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Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive dis-

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Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant

medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

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or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred

vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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CONTENTS

SCIENTIFIC
ARTICLES

Uremic Constrictive Pericarditis. Alexander M. Sloan, Col., USAF MC	1
Unusual Abnormalities Associated with the Floppy Mitral Valve Syndrome. David H. Daniels, Jr., Maj., USAF MC, Umberto D'Ambroso, LTC, USA, MC, and Jules Bedynek, Col., USA, MC	4
Variant Angina Pectoris. Robert M. MacMillan, M.D. and William S. Frankl, M.D.	9
Loose vs Tight Fitting of Silastic Prosthesis of the MP Joint of the Hand. Jonathan A. Lewis, M.D.	15
Asymptomatic Mullerian Anomalies. John L. Currie, Maj., USAF MC	18
The Management of Spine Deformities in the Myelomeningocele Patient. Lyle J. Micheli, Maj., USAF MC and John E. Hall, M.D., FRCS (c)	21
Possible Coagulation Defects Seen in Rocky Mountain Spotted Fever. David A. Driggers., Capt., USAF MC	25

SPECIAL
ARTICLE

Clifton R. Gruver, M.D., President, Medical Society of the District of Columbia	38
Robert B. W. Smith, M.D., F.A.C.P., Editor, Medical Annals of the District of Columbia	41

OTHER
FEATURES

President's Message	5
Individual Consideration. Clifton Gruver, M.D.	
Editorial	6
Colonoscopic Evaluation of Inflammatory Disease. John J. O'Connor, M.D.	
Regarding State Medical Journals, Including Ours. Robert B. W. Smith, M.D., Editor.	
Society Publications. Roger F. Mecum	
Post Graduate Education	45
The Use of Liver Function Tests. Stuart H. Danovitch, M.D.	
The View Box	14
ECG Problems	8
Book Reviews	51
Clinical Electroneurography. (Smorto and Basmajian). Reviewed by Howard M. Silby, M.D.	
Pediatric Otolaryngology. (Ferguson and Kendig) Reviewed by Louis B. Balla, M.D., P.C.	
Statistics in Small Doses. (Castle) Reviewed by James R. Snyder, M.D.	
Major Modalities in the Treatment of Drug Abuse. (Brill and Lieberman). The American Heroin Empire, Power, Profits, and Politics. (Kunnes) Reviewed by Robert DuPont, Jr., M.D.	
The American Medical Machine. (Ribicoff) Reviewed by Elbert T. Phelps, M.D., F.A.C.P.	
Information for Authors	54
Advertising and Subscription Information	58
Index to Advertisers	58

Should children be deprived of milk because of "lactose intolerance?"

No, according to the Protein Advisory Group of the United Nations.

In a special report, the PAG stated, "It would be highly inappropriate, on the basis of present evidence, to discourage programs to improve milk supplies and increase milk consumption among children because of fear of milk intolerance." The statement emphasizes that low lactase activity and results obtained in tests with high lactose loads are not adequate indications of milk intolerance.

The statement also affirms the advisability of using milk as an excellent source of protein in child feeding programs.

Dairy Council is sponsoring further research on lactose intolerance. This is just another of the many areas of interest of Dairy Council, in the pursuit of better health for everyone through sound nutrition practices.

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We would like to take this opportunity to thank Dr. Raymond Scalettar for his fine devotion and help in coordinating and publishing the MEDICAL ANNALS. As Editor of the ANNALS for 1971-1973, Dr. Scalettar contributed greatly to our Society and the D.C. medical community. Our many thanks and best wishes to Dr. Scalettar.

*Dr. Robert B. W. Smith
Mr. F. P. Ferraraccio
Mr. Roger F. Mecum*

Our appreciation to Colonel Alexander M. Sloan, USAF MC, Chairman, Department of Medicine, Malcolm Grow USAF Medical Center, for coordinating this Andrews Air Force Issue.

PRESIDENT'S MESSAGE

Individual Consideration

With the beginning of a new year, 1974, I want to take this opportunity to wish each of you, my fellow members, a Happy, Healthy, and Productive New Year.

Now, as I am writing this editorial, it is Christmastime 1973 and Franc Ferraraccio and I are completing the composition of membership of the 50 standing committees of the Society. This is always an arduous and lengthy task, because we strive for individual consideration of each member's response to the preference requests. Accordingly, each request is carefully reviewed and assignments made respecting those choices as far as possible. We have spent approximately forty-eight man hours on this one task, reviewing some 500 replies. The great majority will receive their designated first choice, and all will be appointed to at least one of their three top picks. Several committees are in great demand, yet permit relatively few openings. "Utilization and Peer Review," for example, (with a total membership of 20), was the number one request on 75 of the questionnaires returned. Some committees have a three-year tenure, deemed advisable for reasons of maintaining continuity and utilizing experience, and therefore have limited quota and turn over slowly (as with the Committee on Ethics and Professional Conduct). The growing number of active members—now 2000—and their increasing interest and activity in Society affairs, makes some system of committee rotation necessary. However, it is difficult to ask a member to change committees if he has indicated it as his only choice and has served on that same committee for several years.

Nearly 50 percent of our membership participate in committee work, and this is a sign of healthy, viable progressive organization. There is no better way to have a continuing dialogue with your fellow-members and the Society's officers and to make your own voice heard, than through these monthly meetings. Committees are the strength of this Society; and the members are the strength of the committees. All major policies and actions are created from their deliberations and directives.



Clif Gruver

DR. CLIFTON GRUVER

Editorial

COLONOSCOPIC EVALUATION OF INFLAMMATORY DISEASE

Colonoscopy is a well established procedure for the diagnosis and treatment of neoplasms. Its value in ascertaining the linear extent of ulcerative and granulomatous disease, however, has not been fully appreciated. It is felt that judicious use of the colonoscope in patients with ulcerative disease extending beyond the range of the rigid sigmoidoscope would be useful. The colonoscope provides both visual and biopsy evidence of the linear extent of the disease process in contrast to x-ray studies which may not show the early changes characteristic of universal ulcerative colitis.

Because of the different prognosis and therapy, a distinction should be made between universal ulcerative colitis, ulcerative proctitis, and granulomatous colitis. This distinction is made possible by colonoscopy and can be often accomplished as an office procedure.

Preparation of the patient is simple and may be carried out at home. A liquid diet for 24 hours prior to colonoscopy, together with a plain water enema the evening prior, and a second plain water enema two hours prior to colonoscopy are usually sufficient

for the patient with inflammatory disease. The use of harsh laxatives is avoided.

The patient is given intravenous valium for sedation and the procedure initiated. X-ray control is not necessary for the average diagnostic colonoscopy. Force is never applied and usual control is maintained at all times. With the ACMI 9000 PL coloscope, biopsy is possible and multiple level biopsies can be obtained.

Colonoscopy has been used in five (5) young adults recently who had sigmoidoscopic evidence of ulcerative disease. The barium enema, however, was inconclusive for universal disease. Because of the virulence of the symptoms further x-ray was considered, but because of the possible genetic effects of repeated and prolonged x-ray exposure colonoscopy was elected. Three patients were found to have only ulcerative proctitis and two patients were noted to have ulcerative colitis.

Colonoscopy offers a new modality in the diagnosis of colonic disease. It is a safe procedure if used properly and avoids the genetic dangers of prolonged and repeated x-ray.

JOHN J. O'CONNOR, M.D.

Regarding State Medical Journals, Including Ours

Dr. Burka, in his President's address in November, referred to decisions that the membership of this society may have to make in regard to the Medical Annals and the News Letter, chiefly because of problems arising from increasing costs. Recently, several of the state journals have quietly folded, in part because advertising money from the pharmaceutical industry is being diverted into their own throw-aways, and because advertising and other money is generally tight.

The state journals have to compete—or try to—with major national journals for scientific material and advertising, and must compete for articles with relatively well-funded pharmaceutical company publications, most of which are professionally

polished and illustrated. The Medical Annals, of course, is unusual among the state journals in that it is almost entirely "scientific", with the News Letter carrying the short-fuse communication, but it shares the problems of obtaining papers and money.

With all their problems, why bother with state journals anyway? The usual answer is that these journals are justified on the grounds of tradition or prestige, as teaching tools, or in order to more-or-less permanently record medical data. The last two reasons, I think, are very valid ones.

Regarding teaching, no one journal, even the best and broadest weekly (NEJM or Lancet, for example) can possibly teach all things to all men. Even a smaller monthly journal can regularly provide

interest, and stimulus, for most readers, with very good original papers, reviews, and some papers of more limited interest. Our medical community is a large one, and we can reasonably expect (if papers continue to be forthcoming) to continue to rival scientific journals from such institutions as the Mayo Clinic. Further, since we are in the gap between the major national and international journals for original scientific papers and the pharmaceutical journals which largely publish predigested material, we are at much greater liberty to encourage young authors. We are obviously an ideal vehicle for publication on community medical problems (which often have a national or international interest).

Our major purpose, however, is to further the advance of scientific knowledge in a very concrete way. There are papers which need to be published, in order to record data, which would not ordinarily be accepted by the major journals. More importantly, there are a great many significant papers which would not be written if we did not ask for them. These papers become part of the body of medical knowledge available on demand to the clinician and investigator, with their worth tested by the reactions of an audience. Without this form of editing by an audience, it would be simple enough to feed unpublished papers into some data-recall computer system where they would be free from the critical eyes of writers of letters-to-editors and colleagues. Far better to let them provide interest to the reader, local or national, and stand on their merits.

Finally, I cannot help but feel that the Medical Annals, in serving a large medical population in a small geographic area, contributes a very great deal to our awareness of being, in fact, a scientific medical community.

Dr. Robert B. W. Smith

Society Publications

At one time the MEDICAL ANNALS OF THE DISTRICT OF COLUMBIA was the only publication of the Society. At that time, it was necessary for the ANNALS to communicate both scientific information and general Society information. The overriding purpose, however, was to allow a printed medium for scientific writing.

The NEWS (Newsletter) came into existence a few years ago, making a second monthly publication mailed to the membership. The NEWS has in recent months grown tremendously and has become the major communicator to the membership of non-scientific information.

Therefore, the ANNALS, as seen in this first issue of 1974, has made the publishing of scientific information its primary role. The journal will serve the medical community of the District of Columbia with Scientific Manuscripts, Special Articles, the President's Message, Editorials, Post-Graduate Education, the View Box, ECG Problems, and Book Reviews.

The monthly features of the past (obituaries, committee reports and new members) will appear in the NEWS beginning with the new year. The NEWS, then, will be a more comprehensive newsletter of all non-scientific information pertinent to the Society. The classified advertising section, formerly appearing in the ANNALS, moved over to the NEWS in August of last year.

The publications of the Medical Society have become more directed, readable, efficient, appealing, and hopefully more meaningful. By making these changes it is hoped the membership will benefit by receiving two monthly publications, each organized and presented in the exact realm of its purpose.

Roger F. Mecum



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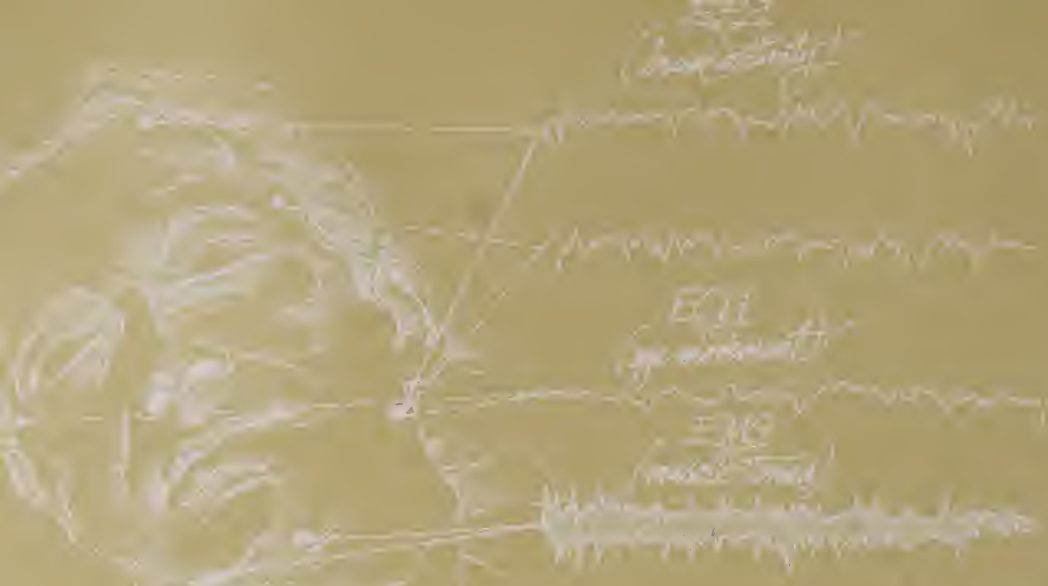
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Contraindications: Known hypersensitivity to flurazepam HCl.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Use in women who are or may become pregnant only when potential benefits have been weighed against possible hazards. Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated, initial dosage should be limited to 15 mg to preclude oversedation, dizziness and/or ataxia. If combined with other drugs having hypnotic or CNS-depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with latent depression or suicidal tendencies. Periodic blood counts and liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdose, have been reported. Also reported were headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins and alkaline phosphatase. Paradoxical reactions, e.g., excitement, stimulation and hyperactivity, have also been reported in rare instances.

Dosage: Individualize for maximum beneficial effect. *Adults:* 30 mg usual dosage, 15 mg may suffice in some patients. *Elderly or debilitated patients:* 15 mg initially until response is determined.

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The American College of Allergists

The Executive Committee of the
American College of Obstetricians
and Gynecologists

The Board of Regents of the
American College of Physicians

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American Dental Association

The Board of Trustees of the
American Medical Association

The American Psychiatric Association

The Executive Committee of the
National Association of Retail
Druggists

The Board of Directors of the
Pharmaceutical Manufacturers
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The National Wholesale Druggists'
Association



Joint Statement on Antisubstitution Laws and Regulations

The purpose of this statement is to affirm the support of the participating organizations for the laws, regulations and professional traditions which prohibit the unauthorized substitution of drug products.

Traditionally, physicians, dentists and pharmacists have worked cooperatively to serve the best interests of patients. Productive cooperation has been achieved through mutual respect as well as a common concern for the ideals of public service. This mutual respect has been reflected, in part, by joint support over the years for the adoption and enforcement of laws and regulations specifically prohibiting unauthorized substitution and encouraging joint discussion and selection of the source of supply of drug products. The basic principles of medical, dental and pharmacy practice are thus utilized and preserved in the interest of patient welfare.

The antisubstitution laws have not obstructed enhancement of the professional status of pharmacy any more than they have in and of themselves guaranteed absolute protection from unsafe drugs, or freed physicians, dentists and pharmacists from their responsibilities to patients. As a practical matter, however, such laws and regulations encourage interprofessional communications regarding drug product selection and assure each profession the opportunity to exercise fully its expertise in drug usage, to the advantage of patients.

Physicians and dentists should be urged to increase the frequency and regularity of their contacts with pharmacists in selection of quality drug products, recognizing that

economies to patients can be improved through such communication, taking into account the patients' needs. The pharmacist's knowledge of the chemical characteristics of drugs, their mode of action, toxic properties and other characteristics that assist in making drug selection decisions should be utilized to the fullest extent practicable by physicians and dentists in serving their patients.

Since drug product selection entails knowledge derived from clinical experience, the physician's and dentist's roles in product selection remain primary and do not permit delegation of decisions requiring medical and dental judgments. A broader role in therapy will evolve for pharmacists as improved understanding and cooperation among the professions continue to grow.

There has been no evidence that there are convincing reasons to modify or repeal existing laws and regulations prohibiting the unauthorized substitution of another drug product for the one specified by a prescriber. It is our belief that such laws and regulations merit the joint support of the medical, dental and pharmaceutical professions and the pharmaceutical industry.

Add your opinion to the weight of other professionals and send it to your state assemblyman or legislator.

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SCIENTIFIC ARTICLES

Uremic Constrictive Pericarditis

ALEXANDER M. SLOAN, COL. USAF MC

Abstract

Despite a high incidence of hemorrhagic pericarditis in uremia (approximately 50%) the development of subsequent constrictive pericarditis is distinctly uncommon in chronic renal failure. With an increased availability of non-conservative means to manage end stage renal disease, as well as Federal subsidy of chronic renal failure treatment, it is reasonable to assume an impending increase in patients utilizing home dialysis. This form of treatment requires the participation of physicians not specifically trained in nephrology, as well as medical center specialists. It should be kept in mind that although uremic constrictive pericarditis is unusual, this case documents the 10th reported patient with constrictive pericarditis successfully treated by surgical intervention in the presence of chronic renal failure. A high degree of suspicion must be maintained for this life threatening but potentially curable condition.

With the recent passage of HR-1 and subsequent increased availability of extracorporeal hemodialysis to patients with end stage renal disease, it is reasonable to assume a parallel increase in patients utilizing home dialysis techniques¹. Since a significant portion of this population's medical care may be rendered by a physician with no in depth training in nephrology it is considered desirable to review the subject of pericarditis, a frequent complication of the uremic state and

emphasize the potential for development of constrictive pericarditis, a surgically correctable condition.

Richard Bright in his classic review published in 1836, noted an 8% incidence of pericarditis and tamponade in acute and chronic renal failure. One hundred years later Ricker and O'Hare² reported the incidence of pericarditis to be 44% of 66 uremic patients, a figure which remains essentially unchanged in more recent series³. Numerous articles have documented the occurrence of tamponade due to uremic pericarditis⁴⁻⁹ and the development of feasible dialytic methods to maintain life in patients with end stage renal disease¹, has stimulated continued interest in this treatable complication. Recurrent pericardial effusion has been treated by surgically creating a pleuropericardial window^{6,8,9} or on occasion pericardiectomy^{8,10}.

The differentiation of constrictive pericarditis from effusion with tamponade can be quite difficult although a progressive decrease in heart size in the face of increasing venous pressure should alert the physician to developing constriction.

Chronic constrictive pericarditis due to uremia, on the other hand, is quite rare and successful surgical management of this complication in patients

on maintenance dialysis has only been reported within the past few years¹¹⁻¹⁶.

The following case report exemplifies the typical evolution of this problem:

Case Report: A 42 year old white male with documented polycystic renal disease of 11 years duration developed the uremic syndrome. Infrequent peritoneal dialysis was employed, but he continued to deteriorate. Symptoms and signs of pericarditis developed during January of 1964 without evidence of significant pericardial effusion. Extracorporeal dialysis was instituted one month later. Following one month of dialysis he developed progressively increasing dyspnea on exertion and peripheral edema. At that time a paradoxical pulse, pericardial friction rub and eight cm. increase in the transverse heart size over that documented five months previously, was noted. Over the next five months he required eight pericardiocenteses with removal from 800 to 1300 cc of sterile bloody fluid for treatment of the symptoms and signs of mild tamponade. At the termination of the eighth procedure 20 mg of prednisolone was injected into the pericardial cavity. Follow-up chest x-rays confirmed the resolution of the pericardial effusion without recurrence.

He remained in his usual state of fair health on twice weekly six to eight hour twin coil dialyses until November of 1965 when his body weight began to gradually increase. The pericardial

UREMIC CONSTRICTIVE PERICARDITIS

SLOAN

friction rub recurred and he began to experience an unexplained low grade fever. Spells of near syncope and recurrence of chest pain typical of his previous pericarditis prompted admission to the hospital in Feb. 1966.

Physical examination on admission showed an oral temperature of 99.3, pulse of 104 and blood pressure of 100/70 without significant paradox detected. The neck veins were distended and the lungs were clear. There was a three component pericardial friction rub loudest at the upper left sternal border with a loud S3 at the apex. A grade 2/6 systolic murmur was present over the precordium, varying with his state of hydration. Large flank masses were palpable and a slightly tender liver edge was felt in the epigastrium 6 cm. below the xiphoid process. A minimal amount of pedal edema was present.

Chest x-ray showed a normal sized cardiac shadow with no evidence of calcification of the pericardium. The EKG showed non-specific ST-T wave changes. Right heart catheterizations demonstrated elevation of the end diastolic right ventricular pressure compatible with myocardial constriction and injection of dye confirmed the presence of thickened pericardium and/or fluid. Ultrasound studies suggested pericardial fluid.

Pericardiocentesis yielded a small amount of bloody fluid which was negative on culture or routine and AFB. The next day following an uneventful dialysis he became hypotensive without response to intravenous volume expansion. Repeated attempts at pericardiocentesis were unrewarding. A day later thoracotomy was performed with the finding of a markedly thickened fibrotic pericardium and very little loculated blood in the residual pericardial sac. The findings confirmed progression to constrictive pericarditis rather than tamponade from fluid. The thickened pericardium was stripped from the

anterior surface of the heart between the left and right phrenic nerves. Immediately following this the left ventricle was seen to expand. Microscopic examination of the resected specimen showed only granulation and fibrous tissue with no granulomas or organisms seen. Culture was again negative. Digitalis started preoperatively was discontinued and convalescence was essentially unremarkable.

The patient remained asymptomatic from the cardiac standpoint for the next three years until he developed sepsis and endocarditis with a fatal termination.

Discussion

Increase in fluid in the pericardial sac over the 25-30cc of straw colored serous fluid normally present occurs in any condition producing generalized edema as well as those conditions producing local inflammation or pericarditis. Cardiac tamponade (compression of the heart by fluid or blood in the pericardial sac) may develop with small volumes of fluid in those cases of rapidly increasing fluid. As little as 150cc of blood can produce an intrapericardial pressure of 15-20 cm of H₂O with fatal results if accumulated rapidly. On the other hand as much as three liters of fluid can be tolerated with little increase in pressure, providing the accumulation occurs over a prolonged period of time.

It has long been recognized that uremia is a frequent cause of pericarditis. Likewise pericarditis is a frequent finding in uremia, the incidence varying between 16% and 45%^{11,17} in dialyzed patients. The exact etiology of uremic pericarditis remains obscure. There is general agreement that preceding major metabolic stress, such as poor biochemical control of uremia sepsis or major surgery is a frequent predisposing factor^{3,11}. Evidence of a direct bacteriologic or viral etiology remains unconvincing with the excep-

tion of infrequently reported cases of septic pericarditis⁸. It would seem that a biochemical abnormality is the most reasonable explanation of this disorder but the exact abnormality remains obscure. As with other manifestations of uremia it is likely that a single "toxin" is not to blame, rather a combination of abnormalities.

The diagnosis of uremic pericarditis is suggested in the following setting: fever, a finding reported in 90% of one series¹¹, pericardial friction rub, chest pain, increasing cardiac silhouette and arrhythmias. EKG changes consisting of ST segment elevations, atrial and ventricular premature contractions, low voltage and non-specific T wave changes were found in 23 of 24 patients in one series¹¹. Radioisotope scanning procedures as well as ultrasound techniques are helpful in most cases. Tamponade is suggested with the development of dyspnea on exertion, syncope, hypotension, increased venous pressure, hepatomegaly and fluid retention.

The treatment of pericardial effusion should be primarily conservative with an increase in the frequency of dialysis initially. Bailly³ reported a 72% incidence of resolution with continued dialysis. Should tamponade occur then pericardiocentesis becomes mandatory. Treatment of recurrent tamponade is usually still feasible by pericardiocentesis; however, in five of 27 patients reported by Kolff⁹ and in two of five patients reported by Hager¹¹, the formation of a pleuro-pericardial window was necessary. The instillation of steroids into the pericardial cavity, as well as the use of systemic steroids^{2,9}, has been recommended. Some benefit may be noted but there seems to be no protection against constriction and one must assume the additional hazards of corticosteroid therapy if given systemically.

In view of the known development of constrictive pericarditis following hemopericardium due to trauma and

the experimental production of constriction by injecting blood into the pericardium of the dog, it is perhaps unusual that the hemorrhagic pericarditis of uremia only rarely progresses to constriction. Experience reported from the Cleveland Clinic⁹ with pericarditis noted complete absence of pericardial calcifications and constrictive pericarditis in 20 autopsied cases. A later review, however¹¹, documents unexpected adhesive pericarditis at postmortem examinations of eight patients treated by chronic dialysis. This would seem to indicate a greater potential for development of constrictive pericarditis than previously thought. Accordingly with increased numbers of patients being dialyzed for longer periods of time constrictive pericarditis may become more frequent. It seems likely, however, that repeated results due to metabolic abnormalities with bleeding and minor degrees of myocardial necrosis is etiologic in the eventual production of constriction. Acute pericarditis with significant effusion has preceded constrictive pericarditis in several cases^{4,11,12,17,18}. The differentiation of constrictive pericarditis from effusion with tamponade can be quite difficult although a progressive decrease in heart size in the face of increasing venous pressure should alert the physician to developing constriction.

Successful surgical treatment of constrictive pericarditis was predicted as long ago as 1895 by Weil. One year later Pick described the syndrome pseudocirrhosis attributed to chronic constrictive pericarditis which bears his name. In 1913 a German surgeon name Rehn performed the first pericardiectomy, and at present a satisfactory result is reported in 86% of pericardiectomies for all causes. This is the tenth case report of successful pericardiectomy for uremic chronic constrictive pericarditis¹¹⁻¹⁶. Additional similar cases have been reported

in small numbers but have either been unsuccessful or have been considered to be subacute constrictive pericarditis¹⁸.

Summary

Uremic constrictive pericarditis is a rare but currently surgically correctable complication of long term dialysis. The clinical picture of increasing venous congestion, decreased cardiac output (frequently manifested as hypotension during dialysis which is unresponsive to the usual volume expansion) and decreasing heart size in a patient with a previous history of recurrent uremic pericarditis should alert the attending physician to this diagnostic possibility. Prompt study and referral to a cardiac surgeon is required if treatment is to be successful.

References

1. KOLFF, W. J., SCRIBNER, B. H.: Panel Discussion, 54th Annual Session American College of Physicians, Chicago, 1973.
2. RICHTER, A. B., O'HARE, J. P.: The Heart in Chronic Glomerulonephritis. *New England Journal of Medicine*, 214, p. 824, 1936.
3. BAILEY, G. L., HAMPER, C. L., HAGER, E. B., ET AL: Uremic Pericarditis: Clinical Features and Management. *Circulation*, 38, p. 582-591, 1968.
4. LINDSAY, S., CRAWLEY, I. S., CALLAWAY, G. M.: Chronic Constrictive Pericarditis following Uremic Hemopericardium. *Amer. Heart Journal*, 79:390-395, 1970.
5. GUILD, W. R., BRAY, M. D., MERRILL, J. P.: Hemopericardium with Cardiac Tamponade in Chronic Uremia. *N. Engl. J. Med.*, 275:5, p. 230, 1957.
6. BARBER, N. D., NAKAMOTO, S., McCORMACK, L. J., KOLFF, W. J.: Pathologic Anatomy of Thirteen Patients after Prolonged Periodic Hemodialysis. *Trans. Amer. Soc. Artif. Int. Organs*, 9:21, 1963.
7. SYMONS, H. S., WRONG, O. M.: Uraemic Pericarditis with Cardiac

- Tamponade: A Report of Four Cases. *British Med. Jour.*, 1:605, 7 Mar 1964.
8. HAGER, E. B.: Clinical Observations on Five Patients with Uremic Pericardial Tamponade. *N. Engl. J. Med.*, 273:6, p. 304, 5 Aug 1965.
 9. BEAUDRY, C., NAKAMOTO, S., KOLFF, W. J.: Cardiac Tamponade in Chronic Renal Failure. *Annals Int. Med.*, 64:5, p. 990, May 1966.
 10. WACKER, W. E. C., MERRILL, J. P.: Uremic Pericarditis in Acute and Chronic Renal Failure. *J.A.M.A.*, 156:764, 1954.
 11. COMTY, C. M., COHEN, S. L., SHAPIRO, F. L.: Pericarditis in Chronic Uremia and its Sequels. *Annals of Int. Med.*, 75: p. 173-183, 1971.
 12. NICKEY, D. O., CHINITZ, J. L., FLYNN, J. J., ADAMS, A., KIRIN, K. E., SCHWARTZ, A. B., ONESTI, G., SCHWARTZ, C. D.: Surgical Correction of Uremic Constrictive Pericarditis. *Annals of Int. Med.*, 75:227-229, 1971.
 13. LONDON, G., JOLY, F., JOLY, H., VALTY, J., GALEY, J. J., MAN, N. K., ZINGROFF, J., AND VANTELONG, J.: Pericarditis Deremiques Constrictives: Deux Nouvelles Observations. *Presse Med.*, 79:341, 1971.
 14. ESMOND, W. G., CHEN LEE, Y., AND HERNANDEZ, F.: Successful Pericardiectomy in Chronic Constrictive Uremic Pericarditis. *South. Med. J.*, 64:533, 1971.
 15. POTTER, D. J., COHEN, A. I.: Diagnosis and Management of Uremic Constrictive Pericarditis. *Ariz. Med.*, 28:302, 1971.
 16. WOLF, S. A.: Constrictive Pericarditis following Uremic Effusion. *J. Thor. Cardio. Surg.*, 63:540-544, April 1972.
 17. MORASKI, R. E., BOUSVAROUS, G.: Constrictive Pericarditis due to Chronic Uremia. *N. Engl. J. Med.*, 281:1; p. 542-543, 4 Sep 1969.
 18. REYMAN, T. A.: Subacute Constrictive Uremic Pericarditis. *Amer. J. Med.*, 46: p. 972-975, June 1969.

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Unusual Abnormalities Associated with the Floppy Mitral Valve Syndrome

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Abstract

The association of a late systolic murmur, non-ejection click, mild mitral regurgitation and billowing of the posterior mitral leaflet is now well documented. This combination of physical findings is commonly referred to as the Floppy Mitral Valve Syndrome. Electrocardiographic abnormalities consisting of T wave changes indistinguishable from inferior wall myocardial ischemia are found in some cases. Chest pain and palpitations are not uncommon and arrhythmias including atrial fibrillation and atrial and ventricular ectopic beats have been observed. Although it has usually been thought of as a benign syndrome, sudden death has been reported. The purpose of this paper will be to point out two distinct abnormalities which have not in the past been emphasized. The first is the association of atypical chest pain, ischemic post exercise electrocardiogram and normal coronary arteries occasionally found in patients with this syndrome. Second is the occasional occurrence of an atrial septal defect. A proposed mechanism for the ischemic post exercise electrocardiogram will be discussed. The clues in the clinical evaluation that led to our suspicion that an atrial septal defect was present in a series of patients will be discussed.

Introduction

The association of a late systolic murmur, mid-systolic click, mild mitral regurgitation, and billowing of the posterior mitral leaflet is now well documented.

Electrocardiographic abnormalities consisting of T-wave changes which are indistinguishable from inferior wall myocardial ischemia are found in some cases. Chest pain and palpitations are not uncommon and arrhythmias including atrial fibrillation and atrial or ventricular ectopic beats have been observed. Although it has usually been thought of as a benign syndrome, sudden death has been reported.

The purpose of this paper will be to discuss associated abnormalities which in the past have not been emphasized.

The first is the apparent association of atypical chest pain, ischemic changes in the post exercise electrocardiogram, and normal coronary arteriography. The second is the occurrence in this syndrome of an atrial septal defect. The following is a case report of a patient studied with atypical chest pain, ischemic post exercise electrocardiogram and normal coronary arteriography.

Case History

H. S., a 46 year old man with a one year history of atypical chest pain

described as a sharp precordial sensation that immediately progressed into a pressure sensation which radiated into the left shoulder and down the entire left arm.

This occurred during exercise and was relieved by nitroglycerin and rest. There was a ten year history of hypertension, but no history of diabetes, smoking or alcohol ingestion. There was no family history of coronary artery disease or diabetes.

The physical examination revealed a well developed white male, in no acute distress, blood pressure was 150/90 mmHg in the arm, pulse 80, and regular with normal jugular venous pulsations.

Precordial palpitation was normal, the first heart sound was normal, the second heart sound was physiologically split, and no atrial or ventricular gallops were heard.

A prominent mid-systolic click was heard along the lower left sternal border with the patient in the sitting position.

A Grade II/VI apical late systolic crescendo murmur was heard; there were no diastolic murmurs. The remainder of the examination was normal. The complete blood count, urinalysis, glucose tolerance test, uric acid and lipoprotein electrophoresis were normal.

The resting electrocardiogram was normal.

The treadmill exercise test revealed

straightening and one millimeter ischemic ST depression two minutes after exercise in leads II, III & AVF.

The patient developed this chest pain during the stress test which was relieved immediately with sublingual nitroglycerin.

Cardiac catheterization revealed normal right and left sided pressure and oxygen saturation. Cine-coronary arteriography was normal. The left ventricular angiogram revealed mild mitral insufficiency and billowing of the posterior leaflet of the mitral valve in the left atrium in systole.

Discussion

The association of the late systolic murmur, non-ejection click, mild mitral regurgitation and billowing of the posterior leaflet of the mitral valve is well documented. The effect of exercise on the electrocardiogram in these patients has received little attention.

Dr. Robert J. Hall and his group at the Texas Heart Institute reported 17 patients with a similar combination of findings⁸. In his series 17 patients presented with chest pain, characteristic ambulatory finding of the floppy mitral valve syndrome and variable electrocardiographic changes at rest. The patients had abnormal post-exercise electrocardiograms which raised a serious consideration of underlying coronary artery disease. In each, coronary cine-angiography was normal and prolapse of the posterior leaflet of the mitral valve was demonstrated. Of the 17 patients, 16 were female and one was male, their ages were 29 through 64 years.

The majority of the patients sought cardiac evaluation because of chest pain alone as did our patient.

Chest pain with palpitations were seen in three of the 17 patients. One was referred because of an abnormal resting electrocardiogram. Some had associated profound fatigue and shortness of breath. Palpitations were a

major complaint in four cases. No patient was referred because of the click or murmur alone.

In our case the patient presented with atypical chest pain, normal resting electrocardiogram, a positive stress test and normal coronary arteriography. The mechanism of the floppy mitral valve syndrome producing chest pain and ischemic ST-T wave changes on the electrocardiogram is unknown.

One group suggested that the billowing posterior leaflet may compromise the circumflex coronary artery causing angina-like pain and abnormal ST-T wave changes. However, this has not been substantiated objectively.

The second unusual abnormality associated with the floppy mitral valve

Normal splitting of the second heart sounds in ASD is extremely uncommon. Nonetheless, the six cases reported herein did indeed demonstrate physiologic variation of the second heart sound with fusion of S2 in expiration.

syndrome is the presence of an interatrial septal defect. Although cases of the floppy mitral valve syndrome in association with atrial septal defect (ASD) have been reported, it has been generally agreed that this association is coincidental¹. Our experience suggests that ASD may represent an associated congenital lesion, since this defect was found in seven of 50 consecutive cases of the floppy mitral valve syndrome seen in our institution. Furthermore, the six cases herein reported are of interest because the diagnosis of ASD was masked, due to the fact that the second heart sound split physiologically and became single on expiration.

Case No. 1

C. G., a 50 year old white woman,

presented with a history of a cardiac murmur noted since the age of seven years. She was free of symptoms until 1967, at which time she experienced shortness of breath and easy fatigability. She subsequently experienced severe congestive heart failure with cardiomegaly, right pleural effusion and ascites and was successfully treated with digitalis and diuretics. Her past medical history was otherwise noncontributory. Physical examination revealed a blood pressure of 140/84 mm. of mercury, and a pulse rate of 60. Cardiac examination revealed the presence of a right ventricular lift and a Grade III/VI apical late systolic murmur, associated with a mid-systolic click. The second heart sound remained split in the supine position but became single on expiration, with the patient in the standing position. A diastolic flow rumble was heard at the lower left sternal border. The electrocardiogram revealed nonspecific ST-T changes consistent with digitalis effect and a roentgenogram of the chest demonstrated a prominent pulmonary artery segment and cardiomegaly. Cardiac catheterization demonstrated a secundum ASD, with a pulmonary blood flow-to-systemic blood flow ratio of 1.9:1. The pulmonary artery pressure was normal. A left ventricular angiogram demonstrated 2+ mitral insufficiency but was otherwise normal.

At surgery, a 1½ cm. secundum ASD was closed by direct suture. A cursory examination of the mitral valve at that time revealed no gross abnormality. However, the mid-systolic click and late systolic murmur persisted.

Case No. 2

G. N., a 36 year old white woman, presented with a history of a cardiac murmur first heard at the age of three years. She did well during her youth and adolescence and subsequently had two uneventful pregnancies. Physical

UNUSUAL ABNORMALITIES WITH FLOPPY MITRAL VALVE

DANIELS, D'AMBROSO AND BEDYNEK

examination demonstrated a blood pressure of 150/80 mm. of mercury and a pulse rate of 76 beats per minute. Cardiac examination revealed a gentle right ventricular lift. The second heart sound split normally with the patient in the sitting position, although a fixed split was noted when the patient was supine. A Grade IV/VI systolic murmur was present at the apex, with radiation to the left axilla. This murmur was almost pansystolic. In addition, several non-ejection clicks were heard at the apex. The electrocardiogram was suggestive of left atrial enlargement, and a roentgenogram of the chest revealed normal lung fields and normal vasculature, but a prominent pulmonary conus.

Cardiac catheterization revealed a secundum ASD with a pulmonary blood flow-to-systemic blood flow ratio of 1.6:1. A left ventricular angiogram demonstrated 2+ mitral insufficiency with ballooning of the posterior leaflet of the mitral valve into the left atrium.

Case No. 3

G. A., a 47 year old white woman, had a questionable history of rheumatic fever at the age of eight, at which time a cardiac murmur was discovered. She experienced excessive weight gain and shortness of breath during subsequent pregnancies and was treated with digitalis. Otherwise, she had been asymptomatic. Cardiac examination revealed a Grade II/VI systolic murmur along the left sternal border. A diastolic flow rumble was present at lower sternal border. The second heart sound was physiologically split and became single with expiration. There was also a systolic murmur at the apex with several mid-systolic clicks.

Electrocardiograms revealed an rsrl pattern in V1 and V4 R, and chest x-ray revealed a prominent pulmonary conus. Cardiac catheterization revealed

a secundum ASD with a pulmonary blood flow-to-systemic blood flow ratio of 2:1.

On 11 October, 1967 surgical closure of a 2 cm. secundum ASD was performed. No gross deformity of the mitral valve was noted.

Case No. 4

C. P., a 21 year old black woman, was in excellent health until the age of 20 when she experienced easy fatigability and decreased exercise tolerance. At the age of 16 she had her first pregnancy during which she had a 75 lb. weight gain. At the age of 19 a routine physical examination including a chest x-ray demonstrated cardiomegaly. There was no history of rheumatic fever. Physical examination revealed a blood pressure of 128/70 mmHg. The neck veins revealed no abnormal pulsations. The lungs were clear to auscultation and percussion. Cardiac examination revealed a left parasternal lift. The first heart sound was of normal intensity. S2 was normally split with patient in sitting and standing positions but splitting became fixed with the patient in supine position. A Grade III/VI systolic murmur and mid-systolic click was present at the apex. There was no diastolic murmur or gallop sounds. Her chest x-ray showed a prominent pulmonary conus, and the electrocardiogram showed an rsrl pattern in V1 and V4 R. Cardiac catheterization demonstrated a secundum ASD with a pulmonary blood flow-to-systemic blood flow ratio 3:1. A left ventricular angiogram demonstrated 2+ mitral insufficiency with a ballooning posterior mitral valve leaflet.

At surgery a three cm. secundum ASD was closed by direct suture. Examination of the mitral valve at the time of surgery revealed minimal mitral insufficiency.

Case No. 5

W. S., a 28 year old white woman, was found to have cardiac murmur at the age of 25. She had been essentially asymptomatic although in the past year had complained of easy fatigability and some dyspnea on exertion. She underwent an uneventful pregnancy at the age of 17. There was no history of rheumatic fever.

Physical examination demonstrated a blood pressure of 124/80 mmHg and pulse rate of 80 beats/minute. The neck veins were flat at 30 degrees. The chest was clear to percussion and auscultation. The PMI was palpitated in the fifth left intercostal space slightly beyond the mid-clavicular line. A left parasternal lift was present. The first heart sound was normal. The second heart sound was widely split but closed normally. An intermittent S4 was present at the apex. A Grade III/VI systolic ejection murmur was heard in the pulmonic area. A Grade II/VI holosystolic murmur was heard at the apex radiating to the axilla.

The electrocardiogram was suggestive of minimal left atrial enlargement, and an rsrl complex was present in V1 and V4 R. The chest x-ray revealed a prominent pulmonary conus and suggestive left atrial enlargement.

Case No. 6

S. B., a 45 year old white woman, had a history of recurrent thrombophlebitis of the lower extremities. At the age of 44 she started complaining of easy fatigability and shortness of breath. Diagnosis of recurrent pulmonary emboli was considered. Right heart catheterization done at another institution showed normal pulmonary artery pressure. Patient was referred to a psychiatrist for care. Because of increasing shortness of breath and fatigue she was referred for evaluation.

Physical examination demonstrated a blood pressure of 170/94 mmHg and

a pulse rate of 74 beats/minute. A prominent left parasternal lift was present. The second heart sound closed normally. The first heart sound was normal. A diastolic flow rumble was heard at the low left sternal border. A late systolic murmur was present at the apex radiating to axilla. Several clicks were also heard.

The ECG was within normal limits. Chest x-ray showed cardiomegaly with prominent pulmonary artery conus. Cardiac catheterization demonstrated a secundum ASD with pulmonary blood flow-to-systemic blood flow ratio of 3:1. A left ventricular angiogram demonstrated a billowing posterior mitral leaflet with modest mitral regurgitation.

Discussion

The reason for fixed splitting of the second heart sound in patients with atrial septal defects is not definitely known^{2,3,4}. However, this auscultatory finding represents the key to the diagnosis of this congenital cardiac anomaly. Braunwald and Aygen² found that in 113 of 118 patients with ASD the A2-P2 intervals varied less than 20 msec between inspiration. Three of the remaining five patients had pulmonary hypertension. Normal splitting of the second heart sounds in ASD is extremely uncommon. Nonetheless, the six cases reported herein did indeed demonstrate physiologic variation of the second heart sound with fusion of S2 in expiration. These six patients had, in addition to a secundum ASD (proven at the time of open heart surgery in four), the floppy mitral valve syndrome. Although we have no explanation for this finding it would seem apparent that the abnormality in the mitral valve apparatus somehow altered this usually diagnostic feature. Hancock and Cohn¹ reported 40 patients with floppy mitral valve syndrome. Two patients in this group were found with typical secun-

dum ASD confirmed by open heart surgery. However, these two patients presented with the usual findings of an atrial septal defect. Four other patients had prominent pulmonary artery segment on routine roentgenography but it is uncertain as to whether hemodynamic data was obtained. Therefore one may speculate as to whether these patients also had ASD's with the usual findings masked by floppy mitral valve syndrome as occurred in our six patients. Additionally our six patients were seen during the course of evaluating 50 other patients with the floppy mitral valve syndrome. This would represent an incidence of 10% which would be much greater than expected by chance association even given that these are two common congenital cardiac defects. Nonetheless this possibility does exist. Another possibility is that these are two separate but somehow congenitally linked defects. It is important to note that all six patients were female.

A final possibility is suggested by the studies of Okada et al⁵. They performed very extensive pathological studies of the heart valves structure in ASD. In 31 cases of secundum ASD, 28 (90%) showed a typical lesion of the mitral valve consisting of thickening of the posterior halves of the anterior and posterior leaflets. Marked thickening of the cordae tendinae near the posterior commissure was also noted. They concluded that these valvular changes were acquired, were not due to rheumatic fever or endocarditis; however were due to continuous hemodynamic stress on the valvular structures. Although they state specifically that mitral insufficiency did not occur, this would seem to remain a possibility. The association of prolapse of posterior cusp of mitral valve and atrial septal defect has been recently emphasized. This association occurred in two of 90 patients reported by Barlow et al⁶. McDonald et al⁷ reported 11 patients with atrial

septal defect and prolapse of the posterior cusp of the mitral valve. They all had the "usual clinical findings of an atrial septal defect."

From analysis of these patients it is suggested that in the evaluation of subjects with floppy mitral valve syndrome, an ASD should be carefully excluded. In doing so the following points are important:

- a). Excessive symptoms
- b). Prominence of the pulmonary artery conus on x-ray
- c). Right ventricular diastolic overload pattern on ECG
- d). A prominent left parasternal lift
- e). Diastolic flow rumble at the left sternal border

These may be the key findings rather than that usually sought for in the diagnosis of ASD, namely a fixed split second heart sound.

References

1. HANCOCK, E. W., COHN, K.: The Syndrome Associated with Midsystolic Click and Later Systolic Murmur, *Am. J. Med.* 41:183, 1966.
2. BRAUNWALD, E., AYGEN, M. M., ROSS, J. JR.: Auscultatory and Phonocardiographic Findings in Atrial Septal Defect in Segal, B. L., Editor: *The Theory and Practice of Auscultation*, Philadelphia 1964, F. A. Davis Co., p 193.
3. LEATHAM, A., GRAY, I.: Auscultatory and Phonocardiographic Signs of Atrial Septal Defect, *Brit. Heart J.* 18:193, 1956.
4. LEATHAM, A.: Splitting of the First and Second Heart Sounds, *Lancet* 2:607, 1954.

UNUSUAL ABNORMALITIES WITH FLOPPY MITRAL VALVE

DANIELS, D'AMBROSO AND BEDYNEK

5. OKADA, R., GLAGOV, S., LEV, M.: Relation of Shunt Flow and Right Ventricular Pressure to Heart Valve Structure in Atrial Septal Defect, *Am. Heart J.* 78:781-795, 1969.
6. BARLOW, J. B., BOSMAN, C. K., POCOCK, W. A., MARCHAND, P.: Later Systolic Murmurs and Non-ejection (Mid-late) Systolic Clicks. An Analysis of 90 Patients, *Brit. Heart J.* 66:443, 1968.
7. MCDONALD, A., HARRIS, A., JEFFERSON, K., MARSHALL, J.,

MCDONALD, L.: Association of Pro-lapse of Posterior Cusp of Mitral Valve and Atrial Septal Defect, *Brit. Heart J.* 33:383, 1971.

8. HALL, ROBERT J.: Chest pain and abnormal post exercise electrocardiogram with normal coronary arteriogram in patients with the click-late systolic murmur syndrome. Presented to the American College of Chest Physicians in Philadelphia, 1971.

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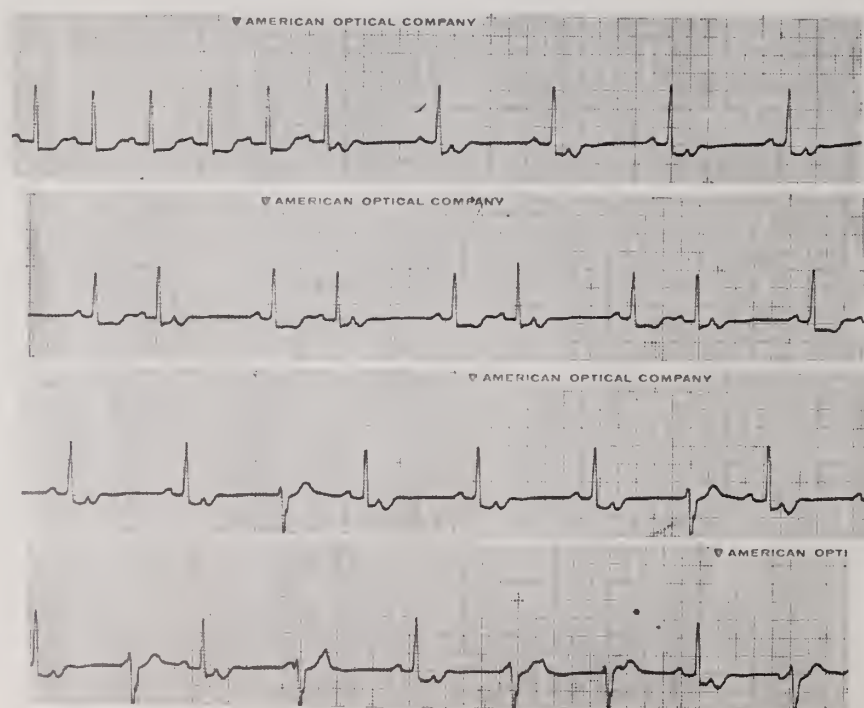
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ECG PROBLEMS

HISTORY: Monitor strips from a patient in CCU on the second day of diaphragmatic wall myocardial infarction. The patient was moderately dyspneic.

(for diagnosis see page 44)



Variant Angina Pectoris

ROBERT M. MACMILLAN, M.D. AND WILLIAM S. FRANKL, M.D.

A 45 year old woman was seen with variant angina pectoris. Included is a case report with the result of coronary angiography.

Printzmetal in 1959 described a distinct variant of angina pectoris¹. The syndrome was characterized by a) pain at rest or with normal physical activity, b) preservation of exercise tolerance, c) ST segment elevation and arrhythmias frequently during the episodes of pain and d) a characteristically good response to sublingual nitroglycerin^{2,3}. Recently Guazzi reported that during the acute episode, cardiac output is decreased, arterial hypotension occurs and systolic time intervals reflect abnormal left ventricular function⁴. Because of the high incidence of subsequent myocardial infarction and mortality in these patients, and the observation that most of these cases involve a single lesion of one coronary artery, coronary angiography has been recommended early in the clinical course^{1,5,6}. Surgical therapy using vein graft bypass has been employed, but numbers remain too few for conclusions as to efficacy of this approach at the present time⁷.

Recently we have seen a case of variant angina pectoris which we have studied and followed through surgery.

Case Report

R. W. is a 45 year old white woman who complained of left anterior and substernal chest pain radiating to both shoulders and upper arms with an aching quality, unassociated with

dyspnea, orthopnea, paroxysmal nocturnal dyspnea, nausea, vomiting, sweating, ankle swelling, palpitations or syncope. The pain had begun one month prior to her first hospital admission in September 1971. It occurred two to three times per week, usually between the hours of 2 A.M.-6 A.M., awakening her from sleep, but occasionally occurring during the day while working in the home. During the attacks of pain she described a habit of getting out of bed and jogging by the

The patient illustrates the presence of atypical anginal syndrome in a normally menstruating woman with no lipid abnormalities, or diabetes mellitus who has developed coronary artery disease in the presence of mild non-treated labile hypertension and adequately treated mild hypothyroidism.

bed which appeared to ease the intensity of the pain. She denied any decrease in her normal physical activity nor any relation to meals.

Past medical history revealed labile hypertension for ten years and borderline hypothyroidism diagnosed in 1960, for which she was receiving Synthroid 0.1 mgm daily. There was no history of antecedent heart disease, diabetes, kidney disease, rheumatic fever or peptic ulcer disease. Although

still menstruating normally, she had had two pregnancies, both leading to spontaneous abortion. She had smoked two packs of cigarettes per day for 25 years but had stopped two years prior to admission.

Physical examination:

Pulse = 76/min. Blood pressure = 150/85. Respirations = 16/min. Temperature = 98°

She was of medium build and well nourished. Examination of the head, ears, eyes, nose and throat were normal, including normal funduscopic findings. There were normal carotid pulsations, no thyroid enlargement and no jugular venous distention at 30°. Pulmonary examination was normal. Examination of the heart revealed an apical impulse in the fifth intercostal space in the midclavicular line. There were no heaves or thrills. There was a grade I/VI systolic ejection murmur heard at the apex and left sternal border. The second sound at the pulmonic area was split physiologically. A₂ was louder than P₂. No atrial or ventricular gallop sound was heard. Rhythm was regular.

The abdominal and neurologic examinations were normal. The extremities were normal with no edema or phlebitis, and pulses were easily palpable throughout.

Laboratory data included: Hgb: 15 gm. %, Hct: 44%, WBC: 8,900 with normal differential, BUN: 15 mgm %, FBS: 80 mgm %, 2 hr. postprandial: 105 mgm %, creatinine: 1.0 mgm %, Na: 141 meq/L, K: 4.6 meq/L, CL: 103 meq/L, CO₂: 24 mM/L, albumin:

VARIANT ANGINA PECTORIS

MACMILLAN AND FRANKL

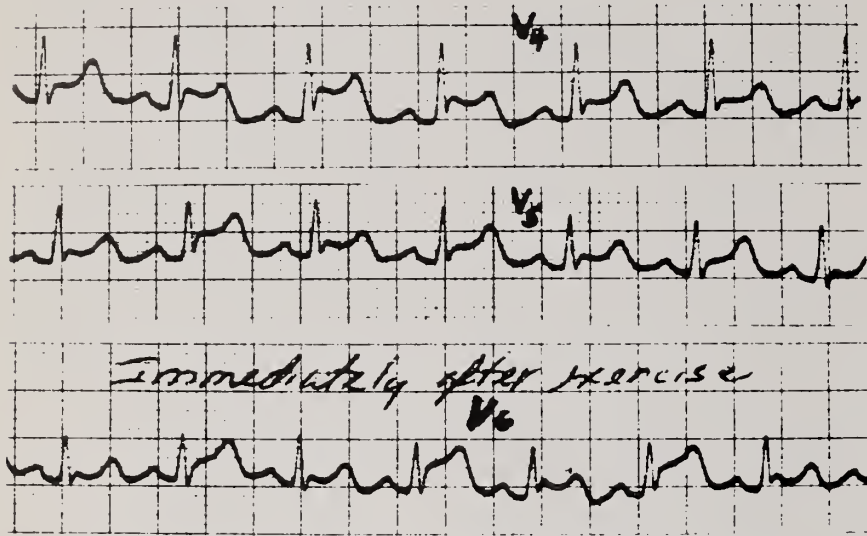


FIG. 1. Post exercise electrocardiogram showing leads V_{4-6} . Note the ST segment elevation which occurs in an alternating pattern in V_6 .

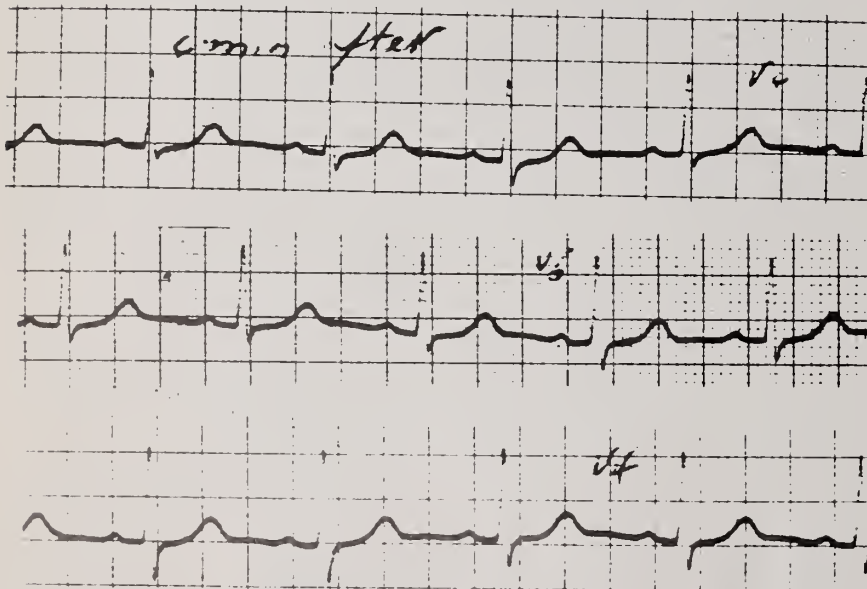


FIG. 2. Leads 4-6 of standard electrocardiogram done 6 minutes after exercise test reveal the return of ST segments to baseline.

4.3 gm %, globulin: 3.0 gm %, SGOT: 34 (normal 0-40), SGPT: 5 (normal 0-20), LDH: 175 (normal up to 200), CPK: 70 (normal 0-130), total bilirubin: 0.5 mgm %, T_4 (Murphy-Pattee): normal, cholesterol: 220 mgm % (normal up to 250), triglycerides: 120 mgm % (normal 30-140), normal lipoprotein electrophoresis. Upper G.I. series revealed a small hiatal hernia. Bernstein's test was negative. Chest x-ray, barium enema and oral cholecystogram were normal. The resting electrocardiogram was within normal limits. A double Master exercise tolerance test was performed and at the end of the test the patient complained transiently of chest "discomfort." Her immediate post-exercise electrocardiogram revealed ST segment elevation in V_{4-6} (fig. 1), and ectopic atrial and ventricular contractions. The ECG done 6 minutes after exercise shows return of ST segments to normal (fig. 2). She was subsequently discharged from the hospital on Propranolol 20

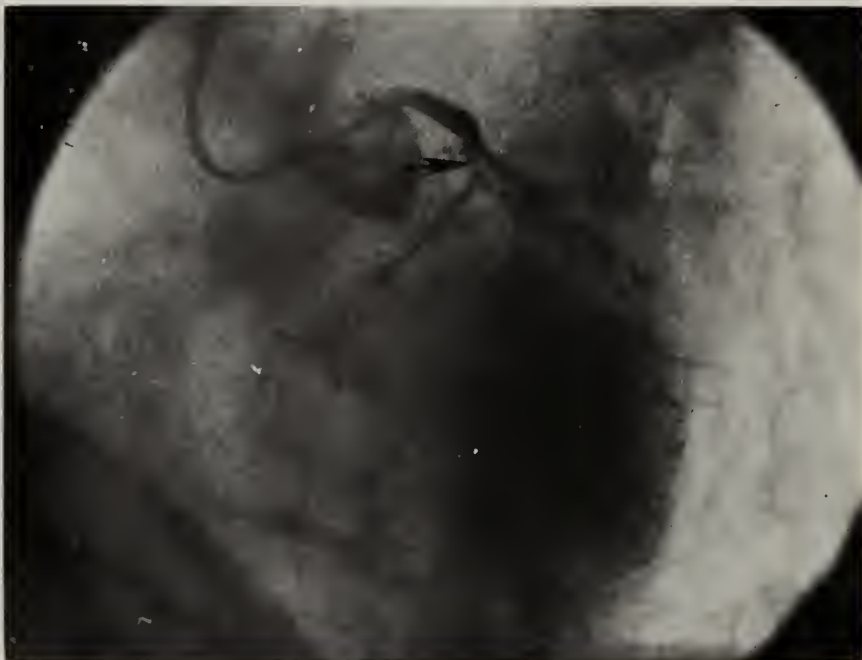


FIG. 3. Left coronary arteriogram in LAO. The arrow marks the site of narrowing of the proximal anterior descending coronary artery.

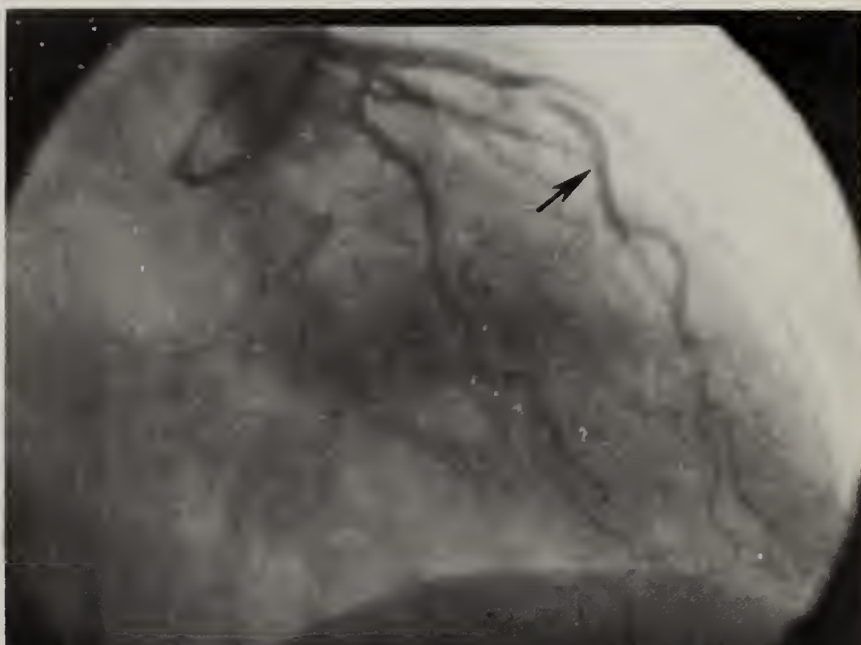


FIG. 4. Left coronary arteriogram in RAO. The arrow marks the site of narrowing of the proximal anterior descending branch of left coronary artery.

mgm q.i.d., Isosorbide dinitrate 5 mgm sublingually q.i.d., nitroglycerin sublingually as needed, and Coumadin 7.5 mgm daily. She was readmitted one month later for coronary angiography when the therapy failed to halt the increasing frequency of attacks. Her resting electrocardiogram was again within normal limits. Right and left selective coronary angiography revealed a single obstructive lesion of greater than 85% narrowing of the proximal 1 cm of the left anterior descending coronary artery (fig. 3-6). Because the patient had never been observed during a spontaneous episode of pain, she was monitored nightly. One evening she had pain at 2 A.M. and her electrocardiogram revealed 4 mm ST elevation (modified MCL¹) associated with ectopic ventricular contractions, some occurring in sequence (fig. 7).

She was referred for coronary artery by-pass surgery, which corroborated the angiographic findings.

VARIANT ANGINA PECTORIS

MACMILLAN AND FRANKL

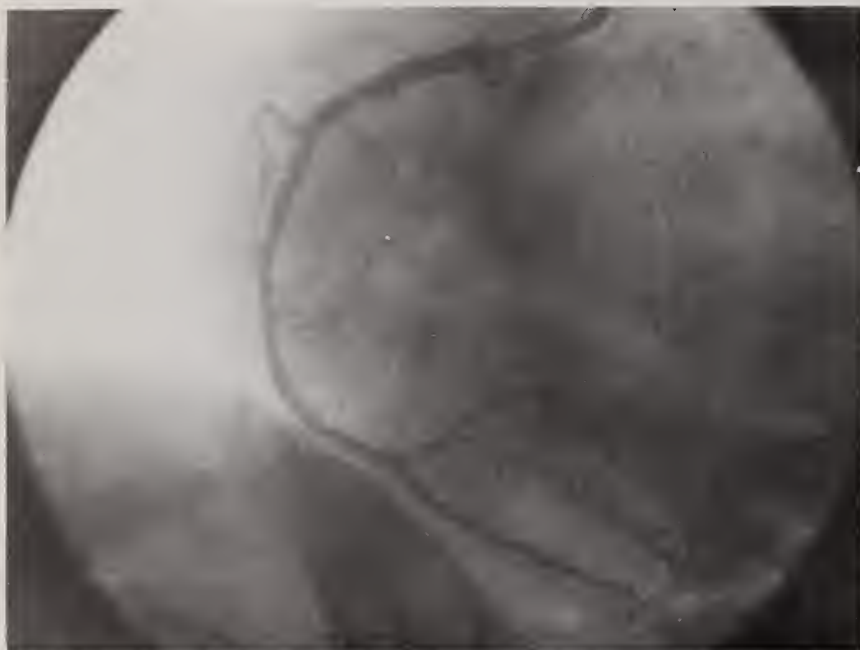


FIG. 5. Right coronary arteriogram in LAO. No evidence of narrowing is seen.



FIG. 6. Right coronary arteriogram in RAO. No evidence of narrowing is seen.

Discussion

This patient illustrates the presence of atypical anginal syndrome in a normally menstruating woman with no lipid abnormalities, or diabetes mellitus who has developed coronary artery disease in the presence of mild non-treated labile hypertension and adequately treated mild hypothyroidism.

It is of some interest to us that her exercise test was grossly positive, contrary to the "classical" Prinzmetal description, and revealed alternating height of ST segment elevation for a considerable period. We do not know the significance of this ST segment electrical alternans.

As regards therapy in this case, we are aware of Guazzi's report of using Propranolol in doses as high as 480 mgm per day in 5 patients with apparently gratifying results⁸. However, we believe that the more definitive surgical approach effected in a semi-urgent manner is more desirable in this form of angina pectoris because of the apparent high incidence of acute myocardial infarction and death in this group as compared to more classical forms of angina pectoris, especially where standard medical therapy does not effect total and rapid relief.

References

- PRINTZMETAL, M., KENNAMER, R., MERLISS, R., WADA, T., BOR, N.: Variant form of angina pectoris. *Am. J. Med.* 27:375, 1959.

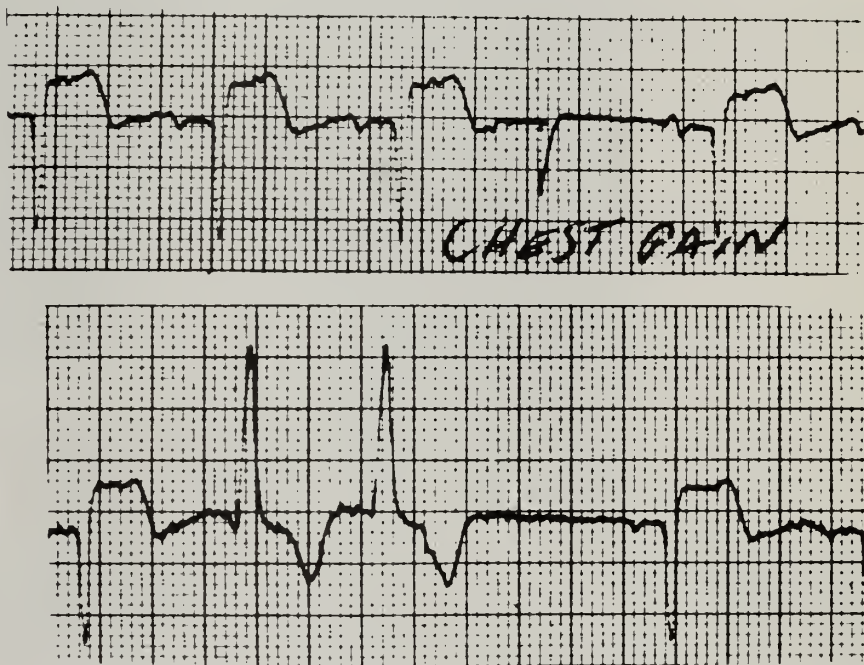


FIG. 7. MCL₁ rhythm strip taken during spontaneous nocturnal chest pain. Note the ST elevation and PVC's.

- BOTTI, R. E.: A variant form of angina pectoris with recurrent third degree A-V block, *Am. J. Cardiol.* 17:443, 1966.
- WHITING, R., KLEIN, M., VANDER VEER, J., LOWN, B.: Variant angina pectoris, *N. Engl. J. Med.* 282:709, 1970.
- GUAZZI, M., FIORENTINI, C., POLESE, A., MAGRINI, F.: Continuous EKG recordings in Prinzmetal's variant angina. *Brit. Heart J.* 32:611, 1970.
- FORTUIN, N. J., FRIESINGER, G. C.: Exercise induced ST segment elevation. *Am. J. Med.* 49:459, 1970.
- MACALPIN, R. N., KRATTUS, A., Jr.: Angina pectoris at rest with preservation of exercise capacity. *Circulation*. 36 (Suppl. II):176, 1967.
- SILVERMAN, M., FLAMM, M.: Variant angina pectoris. *Ann. Int. Med.* 75:339, 1971.
- MARRIOTT, H. J., FOGG, E.: Constant monitoring of cardiac dysrhythmias and block. *Mod. Concepts of Cardiovasc. Dis.* 39:103, 1970.
- GUAZZI, M., MAGRINI, F., FIORENTINI, C., POLESE, A.: Propranolol and Prinzmetal's variant angina. *Brit. Heart J.* 33:889, 1971.

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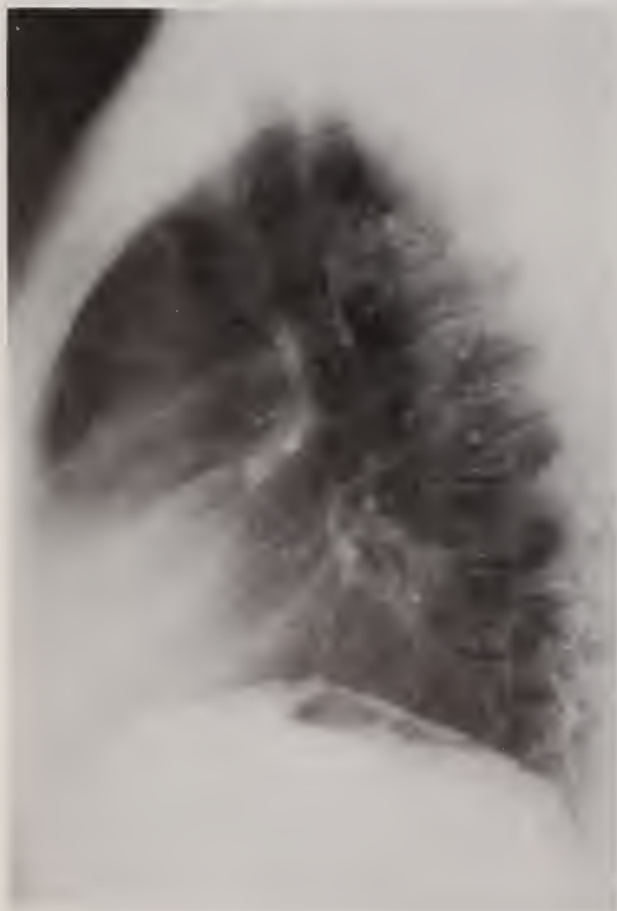
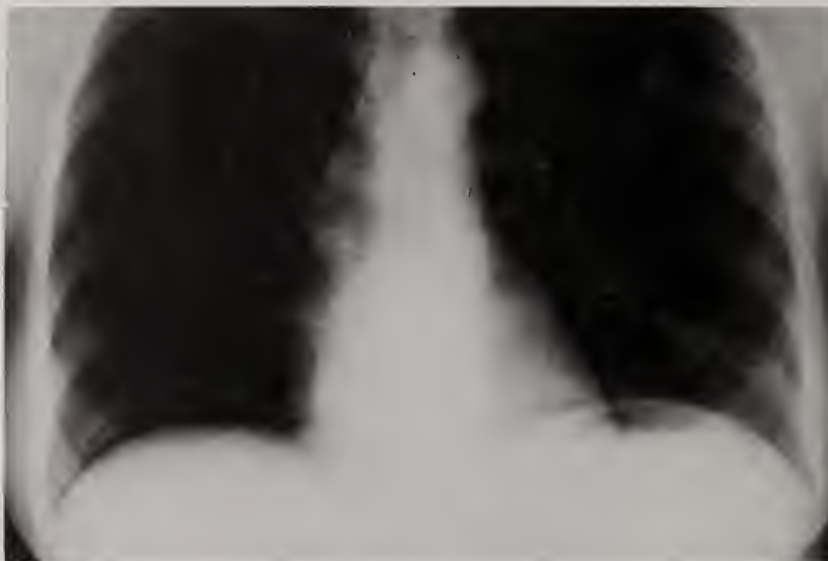
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THE VIEW BOX

Prepared by
The Department of Radiology
Washington Hospital Center

A 28 year old female is admitted with a slowly increasing mass seen on a routine chest radiograph. She has a heart murmur but no significant symptoms.



(for diagnosis see page 44)

Loose vs Tight Fitting of Silastic Prosthesis of the MP Joint of the Hand

JONATHAN A. LEWIS, M.D.

Silastic joint replacements in the hand have been in use for the past eight years for treatment of arthritic deformities. The effectiveness of these silastic joint replacements has been recently evaluated at various centers in cooperation with Dr. Alfred Swanson, who initially developed the silastic prosthesis. The silastic prosthesis has been shown to help in maintaining joint space and alignment, allow joint motion with stability, to be resistant to stress and to be acceptable *in vivo*.¹ The prosthesis consists of intramedullary stems which go up each shaft. These stems do not become fixed to the bone in the Swanson MP silastic prosthesis which is the subject of this report.

In 1971, the author evaluated nine patients (11 hands) with deformities resulting from rheumatoid arthritis and noted fair results in silastic MP joint replacements.² Subsequent to this initial study the author has studied certain changes in the surgical technique of silastic MP arthroplasty which have produced improved results.

Method

The factors evaluated in these patients pre- and post-operatively were range of motion of the joints, degree of ulnar deviation, Boyes measurement (i.e., distance between the finger-tip and palm at full flexion of the fingers) and the patient's and physician's evaluation of the function.

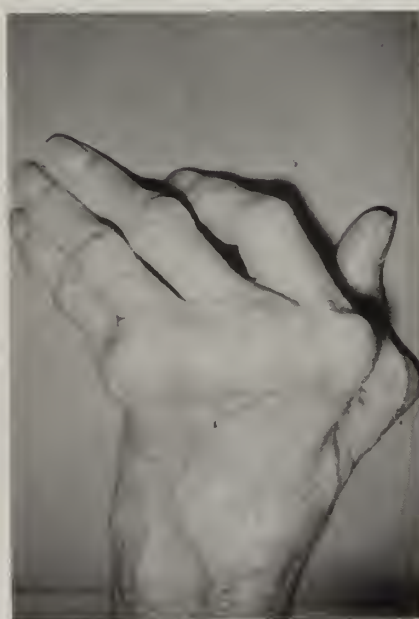


FIG. 1. Patient M. C. preoperative.

The basic surgical technique and surgical indications were performed as described by Swanson.³

Results

It is important to provide stability of the joints as well as movements. A technique of placing the prosthesis tightly has been responsible for improvement of the results. By giving the patient more stability in the joints,

Evaluated were 11 hands with deformities resulting from rheumatoid arthritis and fair results were noted in silastic MP joint replacements.

which occurs with a large tight prosthesis, I have noted that the patients are able to flex their finger-tips to their palm in the past 3 consecutive patients, and have improved strength in pinch in such important activities as writing and holding eating utensils. Thus, these three patients have all been classified as good to excellent. The nine previous patients (11 hands) revealed only one patient (one hand) with a Boyes measurement of 0. This one hand was the only good result in the previous study with the remaining hands rated nine fair and one poor. The average Boyes measurement was 3 cm. in the initial study compared with an average of 0.5 cm. when putting the prosthesis in tight. By putting the prosthesis in loose as proposed in the initial study the ROM of the MP joints was not significantly different, but the ROM in the initial study was in a less functional range; i.e., an average 38° (with average range 10-48°). Placing the prosthesis tightly, the average was 40° with a range of 30-70°.

TIGHT SILASTIC PROSTHESIS FOR HAND JOINTS

LEWIS

Ulnar deviation was corrected with all patients and has been consistently maintained except for one patient in the initial study (the one poor result). The results have shown to peak on the operated hands after six to eight months with little further change noted at the longest follow-up of three years.



FIG. 2. Patient M. C. six weeks post operative showing correction of ulnar deviation.

Discussion

The main difference in technique between the two groups of patients has been the effort to place the prosthesis tightly rather than loosely. The proper degree of tightness can be determined by noting slight tension of the intrinsic mechanism at 30° of flexion. This tightness of the intrinsic mechanism apparently results from lengthening of the bone-joint unit with the large prosthesis. Dr. Swanson has stated that the prosthesis should not be tight, but that the prosthesis is



FIG. 3. Patient M. C. six weeks post operative showing full flexion of fingers.



FIG. 4. Patient M. C. six weeks post operative showing active extension of fingers.

designed to undergo a pistoning action with movement of the fingers.⁴ This is to help prolong the life of the prosthesis (although this soon may not be a factor since an even stronger Swanson silastic prosthesis is being tested now). One patient in the initial study had breakage of one MP joint pros-



FIG. A. Swanson silastic metacarpophalangeal prosthesis.

thesis. The initial nine patients (11 hands) had the prosthesis placed loosely, and the last three successive patients have had the prosthesis placed tightly with larger size of silastic joints being used. The changes in technique have improved the results, both from the patient's and physician's point of view, and have also allowed earlier use of the hand.

Summary

Twelve patients (14 hands) have been evaluated pre- and post-opera-

tively for the silastic replacement arthroplasty of metacarpo-phalangeal joints. The follow-up periods have been from 6 months to 3 years.

The results have been evaluated by various parameters and the results have been noted to be very acceptable with only one poor result.

The author has noted that the best results occur when the prosthesis are placed tightly, using as large a prosthesis as possible, and recommends this technique. It is felt that this change in technique provides for greater stability to these joints and helps provide better function.

References

1. DR. A. SWANSON: Surgical Clinics of North America, Vol. 48, No. 5, Oct 1968, pg. 1114.
2. DR. J. LEWIS, DR. K. HEIPLE, DR. E. WECKESSER: Unpublished Report, Silastic M.P. Arthroplasty—University Hospitals Cleveland.
3. DR. A. SWANSON: Orthopaedic Clinics of North America, Vol. 1, Number 2, Nov. 1970, Pg. 292.
4. DR. A. SWANSON: Surgical Clinics of North America, Vol. 48, No. 5, Oct. 1968, Pg. 1118.

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Asymptomatic Mullerian Anomalies

JOHN L. CURRIE, MAJ., USAF MC

During the third month of intrauterine life of a normal female fetus, the paired Mullerian ducts differentiate into the fallopian tubes, uterus, cervix, and upper vagina.¹ Fusion of the caudal portion of the ducts and obliteration of the interseptum is essential for formation of a single uterus, cervix and upper vagina. Failure of any steps in Mullerian development leads to the most common group of congenital anomalies in the female genital tract. The purpose of this communication is to present three cases of rudimentary uterine horn formation discovered at the time of routine postpartum sterilization.

The clinical significance ranges from absolute infertility associated with absence of the tubes or uterus, to entirely asymptomatic anomalies such as minor septums in the vaginal area.

Case Material

From July 1, 1969 to July 1, 1973, there were 5,189 deliveries and 2,988 gynecological admissions at the Malcolm Grow USAF Medical Center. During this same four-year period, there were 97,994 outpatient gynecological visits. All inpatient charts which were coded for abnormalities of the Mullerian system were reviewed; the collective results are summarized in Table I. In all there were 12 cases,

TABLE I: Mullerian Anomalies
July 1, 1969-July 1, 1973

Hospital Number	Diagnosis	Age	Operation
216599	Left rudimentary uterine horn	34	Unilateral tubal ligation excision of horn
214992	Right rudimentary uterine horn	29	Unilateral tubal ligation excision of horn
213358	Partial vaginal agenesis with hematocolpos, hematometria	12	Vaginal reconstruction
209938	Bicornuate uterus adenocarcinoma, cervix, Stage I-B	34	Radical hysterectomy pelvic lymphadenectomy
209587	Vaginal agenesis and uterine agenesis	14	Laparoscopy
209500	Right rudimentary uterine horn	38	Repeat Cesarean section, unilateral tubal ligation excision of horn
205118	Subseptate uterus	22	Dilation and curettage
202354	Subseptate uterus partial abruptio placenta	32	Low forceps delivery
195187	Bicornuate uterus habitual abortion	22	Strassman procedure
191687	Vaginal septum	21	Assisted breech delivery
190990	Congenital vaginal restricting ring	24	Repair of ring
187909	Vaginal septum	22	Excision of septum

an incidence of one in 249 gynecological admissions.

Three patients (25%) were found to have an anomaly of the uterus at time of postpartum sterilization. The reproductive history of these patients is summarized in Table II. In all cases the asymptomatic horn had the appearance of a "knob" or myoma. Careful inspection, however, revealed (a) insertion of the round ligament into the protrusion, (b) absence of a well-

defined fallopian tube, (c) a normal ovary with insertion of the ovarian ligament into the horn, (d) presence of a fimbrial fragment at the location of the fimbria ovarica, and (e) normal development of the contralateral uterine horn, tube, and ovary. In all cases, the asymptomatic horn was completely excised, the round ligament used to cover the defect, and a Pomeroy tubal ligation performed on the normal tube. In the third case the

suspected diagnosis was confirmed by hysterosalpingography (Figure 1). All patients experienced normal postoperative courses. Pathologically, two of the specimens were composed of only smooth muscle; the other, however, contained scattered endometrial glands with a pseudodecidual reaction present.



Fig. 1. Hysterosalpinogram of patient B. A. Only the left horn of the uterus fills with contrast; the tubal lumen fills to the point of surgical ligation.

Approximately 75% of women with Mullerian abnormalities will exhibit symptoms.² The most common gynecological problems include dysmenorrhea, irregular bleeding, menorrhagia, and infertility. In a series of 75 obstetric patients with various Mullerian abnormalities, Lewis and Brant³ reported an abortion rate overall of 34.3%, breech delivery in 7.5% (not including those delivered by cesarean section), cesarian section in 24.6%, and normal delivery in only 32.1%. In those pregnancies which went to viability, there was a perinatal loss of 28%.

Rudimentary horns are much less likely to cause symptoms and indeed are usually discovered accidentally. Although dystocia resulting from an incarcerated uterine horn in the pouch

of Douglass has been reported³, obstetric complications directly related to such a horn are unusual. Because unilateral carcinoma of the endometrium in a bicornuate or double uterus has been reported^{4,5}, complete excision of asymptomatic uterine horns is advisable. If the horn contains epithelial elements, a clinical picture resembling endometriosis or adenomyosis may cause a horn to become quite painfully symptomatic. More advanced development of a noncommunicating horn can lead to hematometra and an abdominal mass.⁶

Concomitant abnormalities of the urinary tract frequently accompany even the most minor Mullerian abnormalities. Intravenous pyelography should be performed on all such patients.

Discussion

Because of the intricacies of the development and differentiation of the Mullerian system, an almost infinite variety of congenital abnormalities is possible. Two groups of anomalies are most common: (1) those caused by failure of development, either partial or complete, resulting in absence of one or both fallopian tubes, the uterus, cervix, or upper vagina; and (2) those resulting from the failure of complete obliteration of the septum formed by midline fusion of the ducts, with duplication of the uterus, cervix and vagina, either partial or complete (Figure 2).

The clinical significance of the various abnormalities outlined above ranges from absolute infertility associated with absence of the tubes or uterus, to entirely asymptomatic anomalies such as minor septums in the vaginal area.

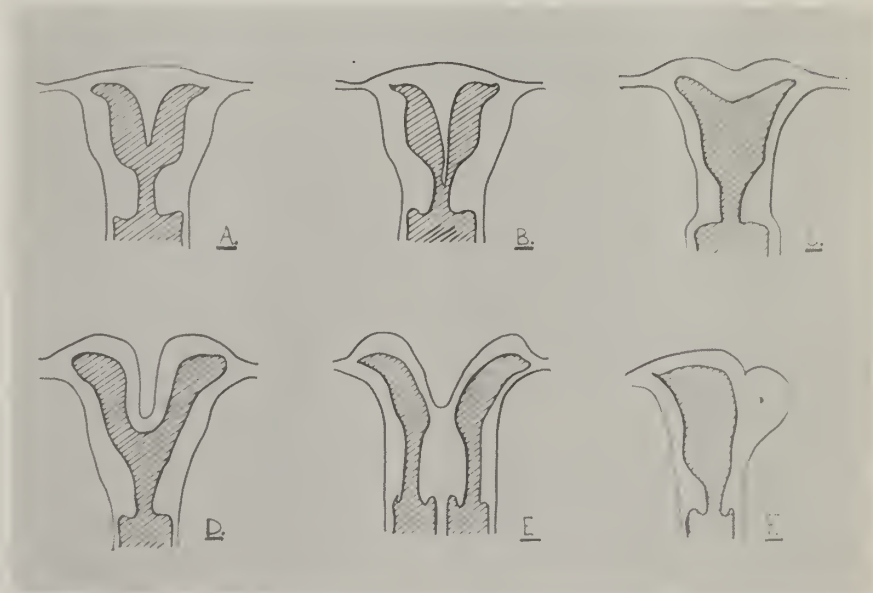


Fig. 2. Schematic diagram of uterine duplications (a) Subseptate uterus (b) Septate uterus (c) Arcuate uterus (usually of little clinical significance) (d) Bicornuate uterus (e) Double uterus, cervix and vagina (uterus didelphys) (f) Rudimentary uterine horn with normal development of contralateral side; the endometrial cavity may be absent, primitive or fully functional. [Modified from Green, T. H., Jr., *Gynecology, Essentials of Practice*, ed. 2, Boston, 1971, Little, Brown and Company, Inc., p. 67].

ASYMPTOMATIC MULLERIAN ANOMALIES

CURRIE

TABLE II

Patient	Age	Grav- ity	Par- ity	Spontan- eous Abor- tions	Comment	IVP
B. N. 209500	38	4	3	1	Spontaneous delivery, 1955 Cesarean section, placenta previa, 1958 Spontaneous abortion, 1961 Rudimentary horn excised after repeat Cesarean section, 1972	Normal
M. B. 216599	33	3	3	0	Postpartum hemorrhage with second delivery First and third deliveries normal	normal
B. A. 214992	29	3	3	0	Left accessory nipple ex- cised at the time of tubal ligation	normal

Summary

Three patients with asymptomatic rudimentary uterine horns discovered at the time of postpartum sterilization are presented. The more clinically significant types of Mullerian abnormalities are briefly outlined.

References

1. NOVAK, E. R., JONES, G. S., JONES, H. W. JR.: *Novak's Textbook of Gynecology*, 7th ed. Baltimore: The Williams and Wilkins Company, 1965, 114, 115.
2. GREEN, T. H., JR.: *Gynecology, Essentials of Practice*, 2nd ed. Boston: Little, Brown and Company, Inc. 1971, 67.
3. LEWIS, B. V., BRANT, H. A.: Obstetric and gynecologic complications associated with Mullerian duct abnormalities. *Obstet. Gynec.*, 1966, 28, 315.
4. BRAUN, D. R.: Uterus didelphys and endometrial carcinoma. *Obstet. Gynec.*, 1970, 35, 93.
5. DAVIES, S. D., NISBET, J. D.: Uterus didelphys with adenoacanthoma involving one cavity. *Amer. J. Obstet. Gynec.*, 1972, 112, 1134.
6. JONES, H. W., JR., WHEELLESS, C. R.: Salvage of the reproductive potential of women with anomalous development of the Mullerian ducts: 1868-1968-2068. *Amer. J. Obstet. Gynec.* 1969, 104, 348.

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The Management of Spine Deformities in the Myelomeningocele Patient

LYLE J. MICHELI, MAJ., USAF MC AND JOHN E. HALL, M.D., FRCS(C)

Introduction

Due to dramatic advances in recent years in the neurosurgical and urologic care of patients with myelomeningocele, the orthopaedic surgeon is being presented with increasing numbers of children requiring careful management of complex musculo-skeletal deformities.

Advanced neurosurgical techniques, including immediate closure of the dural defect at birth¹, and early diagnosis and shunting procedures for the associated hydrocephalus, which occurs in approximately 70% of these children², have resulted in a significant increase in neo-natal survival. Urinary diversion procedures, usually employing ileal loop by-pass, are used successfully to treat the obstructive uropathies which develop in the older, more severely involved of these children³.

Initially, Orthopaedic management of these children was directed to the difficult foot and hip deformities seen in a high percentage of these patients, often evident at birth or developing in the first few years of life. More aggressive and earlier Orthopaedic treatment has resulted in plantar-grade feet and balanced hips in an increasing percentage⁴.

However, it is becoming evident that the high incidence of progressive spinal deformities in a significant number of these patients as they get older can jeopardize the entire therapeutic program. A study done at the Newing-

ton Children's Hospital, in Connecticut, in 1970, revealed that 62% of the children in their Myelodysplasia Clinic had a spinal curvature of greater than 20°⁵. One eighth of these had a kyphotic deformity, present at birth, and usually progressive. The remainder of these showed evidence of lordosis and lardo-scoliosis usually appearing

In the majority of myelomeningocele patients with spinal deformities, those with lordosis and lardo-scoliosis, the more traditional techniques of posterior spine fusion have frequently given disappointing results . . . a more satisfactory technique of surgical correction and fusion of deformed spines seems necessary.

before the age of five years, and progressing thereafter.

This paper will review several of the newer approaches to treatment of these two types of spinal deformities in patients with myelomeningocele, as seen in the management of two of our recent patients.

Case Reports

1. Patient 1: P.M.

This ten year old girl was the product of a full term normal preg-

nancy without complications. She was noted at birth to have a thoracolumbar myelomeningocele which was closed surgically shortly after birth. At age six months she had a ventriculo-atrial shunt procedure because of slowly progressive hydrocephalus. At age four years, she underwent bilateral cutaneous ureterostomies because of recurrent urinary infections. This procedure resulted in improved renal function and a significantly decreased incident of urinary infections. She has since had one revision of her ventriculo-atrial shunt and one revision of her uretero-cutaneous fistula. She had also had a surgical correction of equinovarus deformity of her right foot at age six years. Her level of effective neurologic function was L₁, confining her to a wheelchair, but she functioned well, and was doing well in school until approximately one year prior to our evaluation when a progressive lardo-scoliosis began to limit her sitting and wheelchair tolerance, and appeared to be contributing to mechanical block at the outflow sites of her uretero-cutaneous fistulae.

At the time of her admission to the Children's Hospital Medical Center in Boston, she demonstrated a long, rigid lardo-scoliotic spinal curvature extending from the fifth dorsal vertebrae to the fourth lumbar vertebra and measuring 132°. An X-ray obtained while traction was applied to the spine and a corrective force applied to the apex of the curve resulted in correction of the

SPINE DEFORMITIES IN MYELOMENINGOCELE

MICHELI AND HALL

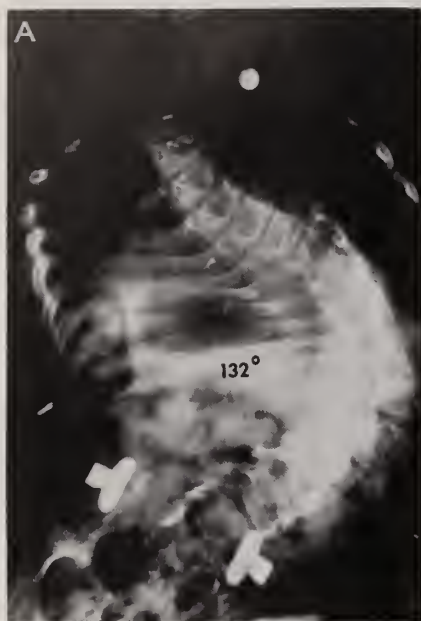


FIG. 1A. P.M. Pre-operative AP X-ray of dorsolumbar spine from the fifth dorsal vertebra to the fourth lumbar vertebra showing a scoliosis of 132° .



FIG. 1B. P.M. Post-operative AP X-ray showing correction of spinal curvature to 52° after twelve level Dwyer instrumentation and fusion.

curvature to only 75° . Lateral X-ray view of the spine demonstrated an associated dorsal lordosis. Admission urinalysis showed 15-20 WBC/HPF, while urine culture grew *E. coli* and *Pseudomonas*. Serum creatinine was 0.36 mg.%. Ventriculo-atrial shunt was functioning satisfactorily. She was felt to be a satisfactory candidate for anterior spinal fusion using Dwyer instrumentation. Post-operative X-ray of her twelve level fusion revealed correction to 52° of her scoliotic deformity. The lateral X-ray showed a similar correction of her dorsal lordosis. She was maintained on bed rest for a two week period and then placed in a light plaster jacket, and resumed her sitting activities.

2. Patient 2: M.L.

This 2-11/12-year child was noted at birth to have a thoraco-lumbar myelomeningocele. She had immediate primary closure of the spinal defects and required a ventriculo-atrial shunt two weeks later because of progressive hydrocephalus. She has since had three revisions of her ventriculo-atrial shunt. In addition, she had adductor myotomies and closed reduction of bilateral dislocated hips at six months of age.

She was noted to have a thoracolumbar kyphotic deformity of the spine at birth, which initially was felt to be stable, but which began to progress significantly in the year prior to evaluation, apparently in association with assuming a sitting position. This progressive deformity had resulted in several skin ulcerations, and progressive difficulty with sitting in the months immediately prior to evaluation.

At the time of initial evaluation, she was an alert child in no significant distress. Head circumference was 48 cm. chest and abdominal examination were normal. She could maintain a sitting position only with support, and demonstrated a dorsolumbar kyphosis

extending from approximately T-10 to L-5 with thinning of the overlying skin. Motor examination showed her to be flail below the hips, with a sensory level at approximately the L-2 dermatome. It was decided that the patient would benefit from a posterior resection of the kyphotic portion of her spine and primary fusion. At operation, a posterior wedge resection including the entire third lumbar vertebra and one half of the second vertebra above and the fourth vertebra below, with the associated disc spaces, was performed.

Care was taken to preserve the overlying remnants of neural tissue

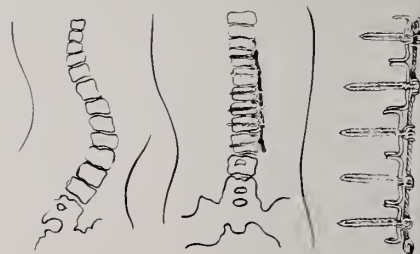


FIG. 2. Correction of Lordo-scoliotic deformities using Dwyer instrumentation is attained by applying a compression system of titanium cable, screw and saddle plates to the convex surface of the curve, with associated inter-vertebral disc excision and anterior inter-body fusion.

and nerve roots. The spine was immobilized by two stainless steel wires passed through the neural foramina of the second lumbar vertebra and fifth lumbar vertebra and lateral bone grafts were put in place. She tolerated the procedure well and was immobilized post-operatively in a posterior plaster shell. Post-operative radiographs demonstrated a significant correction in the spinal deformity.



FIG. 3A. M.L. Pre-operative lateral spine X-ray showing extensive kyphotic deformity.



FIG. 3B. M.L. Post-operative lateral spine X-ray after vertebral body wedge resection and fusion, showing correction of the kyphotic deformity.

Discussion

In the majority of myelomeningocele patients with spinal deformities, those with lordosis and lardo-scoliosis, the more traditional techniques of posterior spine fusion have frequently given disappointing results. The absence of posterior spinal elements increases the difficulty of posterior instrumentation and fusion. These curves are often quite rigid, with associated bony vertebral anomalies, and often quite resistant to correction by posterior instrumentation or cast techniques. The extent of many of these curves, with the extensive decortication and resultant blood loss, renders their correction formidable procedures. Finally, post-operative immobilization in casts or braces is extremely difficult because of the associated sensory deficit and tendency to skin breakdown.

In reviewing the results of posterior spinal fusion for myelomeningocele at the Hospital for Sick Children in Toronto, Briram, Bobechko, and Hall found that only 16 of their 33 patients had had a good result from posterior spine fusion. They noted the high incidence of complications in these procedures, including a 21% rate of infection and 27% rate of pseudoarthrosis, and reviewed in detail the problems of posterior spine fusion in these children which contributed to their high rate of complications⁶.

In view of these experiences, a more satisfactory technique of surgical correction and fusion of these deformed spines seems necessary. The Dwyer technique of spine fusion, developed by Mr. Allen Dwyer and his colleagues, in Melbourne, appears to hold promise in the treatment of these deformities⁷.

In this procedure, the corrective apparatus is applied to the vertebral bodies, in the front of the spine. In the myelomeningocele patient, the body of the vertebra is usually normal, anatomically, in contrast to the de-

formed and absent posterior elements of the vertebra. The entire disc is excised between each vertebral body, and bone graft placed between the vertebral bodies to obtain fusion. Segmental compression between each vertebral body is applied to the convex side of the curve by a system composed of titanium screws, saddle plates, and cable. The titanium screw is inserted transversely across the body



FIG. 3C. M.L. Post-operative AP spine X-ray showing extent of vertebral body resection and fusion.

of the vertebra, passing through a saddle plate on the convex side of the body to distribute the force. A braided titanium cable is passed through the eye of each screw and wedged into place on the screw after maximum compressive force has been applied between each two adjacent vertebral bodies.

Use of the Dwyer technique to correct the lardo-scoliotic deformities

SPINE DEFORMITIES IN MYELOMENINGOCELE

MICHELI AND HALL

found in myelomeningocele appears to offer several distinct advantages. As noted previously, and most important, it involves an anterior fusion between the bodies of adjacent vertebra, which, in the myelomeningocele, are the only basically normal portions of the involved bony spine. Secondly, blood loss is limited, with an average blood loss of 600 cc per procedure. Blood loss using posterior fusion techniques is often three to four times this. Thirdly, these patients have demonstrated a relatively benign post-operative course. They are often comfortable and sitting by the third post-operative day, and up with a plaster jacket at 10 to 14 days post fusion. Finally, there appears to be a significantly lower incidence of complications using this technique, with a negligible incidence of sepsis and a much higher rate of fusion using this technique than in the posterior correction and fusion technique.

Treatment of those children who develop the second type of spinal deformity seen in the myelomeningocele, dorso-lumbar kyphosis, continues to be a difficult problem. With

progressive deformity, sitting becomes increasingly difficult, with the upper torso and rib cage impinging on the pelvis, interfering with breathing, and sometimes mechanically obstructing ileal conduit drainage. Recurrent skin ulceration over the sharp dorsal gibbus makes supine lying hazardous, and prone lying is often impossible because of the primary spinal deformities and associated hip deformities. Recent experience with early posterior spinal wedge resection and fusion, as detailed by Sharrard⁸, seems to hold promise in the correction of myelodysplasias with this deformity, but more experience with these extensive and hazardous surgical procedures is required, especially as regards the possibility of late recurrence of the deformity, before we can be certain of its ultimate role.

References

1. SHARRARD, W. J. W., ZACHARY, R. B., LARDER, J., BRUCE, A. M.: A controlled trial of immediate and delayed closure of spina bifida cystica. *Arch. Dis. Child*, 1963, 38, 18.
2. ECKSTEIN, H. B., MACNAB, G. H.: Myelomeningocele and Hydrocephalus. The impact of modern treatment. *Lancet*, 1966, 1, 842.
3. MORALES, P. A., DEEVER, C. C., HOTCHKISS, R. S.: Urological complications of spina bifida in children. *J. Urol.*, 1956, 75, 536.
4. MENELAUS, M. B.: The orthopaedic management of spina bifida cystica. Edinburgh, E & S Livingstone, 1971.
5. American Society of Orthopedic Surgeons Symposium on Myelomeningocele, St. Louis, The C. V. Mosby Company, 1970.
6. SRIRAM, K., BOBECHKO, W. P., HALL, J. E.: Surgical management of spinal deformities in spina bifida. *J. Bone & Joint Surgl*, 1972, 54B, 666.
7. DWYER, A. F., NEWTON, N. C., SHERWOOD, A. A.: An anterior approach to scoliosis. *Clin. Ortho. & Rel. Research*, 1969, 62, 192.
8. SHARRARD, W. J. W.: Spinal osteotomy for congenital kyphosis in myelomeningocele. *J. Bone & Joint Surgl*, 1968, 50B, 466.

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Possible Coagulation Defects Seen in Rocky Mountain Spotted Fever

DAVID A. DRIGGERS, CAPT., USAF MC

Abstract

The increased ability of the clinician to recognize and treat coagulopathies in various disease states has become more readily apparent over the past decade. A case of documented Rocky Mountain spotted fever with thrombocytopenia provides the unique question as to what causes the clinical and laboratory evidence for a bleeding diathesis in the presence of vasculitis. In addition a background discussion is presented on the etiology, pathology, clinical signs and symptoms, and the treatment of Rocky Mountain spotted fever.

Introduction

Over the past decade the recognition of consumptive coagulopathies in various disease states has been transferred from the research laboratory to clinical medicine. However, this has not been without problems. First, is the recognition of the disorder in the many clinical settings that it may occur ranging from surgical procedures to serious infections. Secondly, once clinical and laboratory evidence has been obtained which points toward the diagnosis of a consumptive coagulopathy, a decision must be made as to mode of treatment, such as heparin in the face of a bleeding patient. In August 1972 we had the opportunity to treat a patient that brought to the

surface the problems of recognition and treatment of coagulation defects seen in Rocky Mountain spotted fever. This stimulated much research of the literature and it is the purpose of this paper to relate some of the clinical information we obtained to the case presentation and pose some questions as to the diagnostic criteria of consumptive coagulopathies as well as present a discussion of the primary disease.

The importance of a hematologic abnormality is intensified when one considers a ten-fold increase in mortality seen in Rocky Mountain spotted fever in patients with platelet counts of less than 25,000.

Case Report

The patient is a nine year old boy who was in good health until seven days prior to admission when he began running a low grade fever, had nausea and vomiting, malaise, myalgia and anorexia. He was seen in the emergency room five days prior to admission and diagnosed as a non-specific viral illness. Three to four days prior to admission the nausea and vomiting abated but a very fine purpuric rash on his extremities was first noted. The fever persisted, the rash spread to his trunk and face and his sensorium

slowly deteriorated. Also at this time his urine turned dark and his stools became light in color. He then presented to the emergency room with a purpuric rash over his entire body, decreased sensorium, myalgia and fever. At no time did he have arthralgia, shortness of breath, hemoptysis, melena, epistaxis or sore throat. During the summer he was an extremely active boy, playing sports, camping in the woods and keeping up with siblings. There was no history of tick bites, streptococcal infections or travel outside the United States. There was no previous history of rheumatic heart disease, hepatitis, kidney disease, congenital heart disease, bleeding disorders, eczema, asthma or allergies, transfusions and he was on no medications. The family history for bleeding disorders, anemias, infectious hepatitis or other illnesses was negative and the review of systems except for the present illness was negative.

On presentation to the emergency room the patient had a temperature of 102, his blood pressure was 110/80 and his pulse 160. He was awake with a peculiar sensorium, complaining of myalgias and crying frequently. The skin was noted to have a purpuric rash (Fig. 1) that was generalized with increased patches on the extremities especially the palms and soles of the feet and hands. There were no obvious hemorrhages or joint involvement, and the mucous membranes were dry.

COAGULATION DEFECTS IN ROCKY MOUNTAIN SPOTTED FEVER

DRIGGERS



Fig. 1

There was no scleral icterus, the neck was supple and the pharynx benign. The chest, cardiovascular and abdominal exam was normal except for a spleen that was 2 cm. below the left costal margin. The remainder of the physical examination was negative except mild cervical lymphadenopathy. There was no eschar noted. Differential diagnosis on admission included idiopathic thrombocytopenia purpura, septicemia with DIC, collagen disorders, Rickettsial diseases and the hemolytic uremic syndrome.

The immediate problem of fever and sepsis was approached with multiple cultures, gram stains and serologic evaluation, including OX-2, OXK, and OX-19, and because of clinical judgment he was started on intravenous tetracycline at 25 mg/K8 per day. Serology two weeks later confirmed our suspicion with titers of 1:1600 in the OX-2 and OX-19 titers. OXK was negative. The patient gradually improved and except for a superficial elbow ulcer, which grew out

pseudomonas and was treated with topical gentamycin, he was discharged on the 26th day.

The second problem, purpura, was approached with clotting studies including fibrinogen levels, fibrin split products, Coombs test and platelet count. There was no fragmentation of cells in the peripheral smear and clot lysis was negative. The results pointed toward a vasculitis with possible primary platelet consumption, and was then treated with steroids with a gradual increase in platelet count and resolution of the rash.

By the second day of hospitalization the patient began exhibiting pitting edema of the hands and legs, and periorbital edema. By the fourth hospital day this was frank anasarca and serum electrolytes, serum and urine osmolality, urines for sodium and potassium, urinalysis and serum total protein were obtained which revealed only a marked hypoproteinemia. Except for one IV infusion of salt albumin, he was treated expectantly and gradually improved over the following six days.

Discussion

The incidence of Rocky Mountain spotted fever and its associated mortality and morbidity has been increasing in spite of antibiotics. A 50% rise in the reported cases was noted in 1969 with 498 reported to the Center for Disease Control. Of this Virginia led all states with 91, in which a case fatality of 4.4% was noted¹. In 1972, 528 cases were reported with approximately the same case fatality of 5%². The fact that Rocky Mountain spotted fever is primarily a disease of the South Atlantic states is contrasted by the fact that it was first described in 1898 by Wood in Boise, Idaho although not fully appreciated until 30 years later (Fig. 2). The primary vector is the American dog tick, *Derm-*

centor variabilis, which parasitized the white footed deer mouse, host for the *Rickettsia rickettsiae*³. Once introduced into the human the rickettsiae attack small vessels of the skin and subcutaneous tissue resulting in monocytic and polymorphonuclear infiltration of the endothelium. Secondary thrombotic formation and vascular necrosis occurs giving a classic picture of fever, headache and rash three to ten days after tick exposure⁴. The majority of the cases occur in the summer months from May through July and usually in the two to ten year age group³. The major symptoms seen are rash, headache, vomiting, myalgia and lethargy^{4,5}. The clinician should then note rash usually seen on the flexor surface of the extremities, fever, periorbital edema, splenomegaly and abdominal tenderness. Serologic studies should include complement fixation and serology for proteus OX-19, OSK and OX-2 with an OX-19 titer greater than 1:320 or a complement fixation level greater than 1:8 considered to be diagnostic ten days after infection.

The most important immediate differential diagnosis should be meningococcal meningitis, neurologic manifes-

FIG. 2. Tick-Borne Typhus, 1969-States Having Incidence Greater Than 1 of 200,000 Population¹

State	Rate Per 100,000*
Virginia	1.94
North Carolina	1.28
Maryland	1.27
Oklahoma	1.24
South Carolina	1.18
Tennessee	1.07
Idaho	0.83

* Population figures based on July 1, 1969, estimate by US Bureau of the Census.

tations include lethargy, meningismus, delirium and confusion, with associated spinal fluid changes including increased protein, red blood cells and leukocytes. However, in Rocky Mountain spotted fever the gram stain is negative and the glucose level is usually normal. The meningococcal skin rash, whether acute or chronic, may be similar to Rocky Mountain spotted fever, being macular, papular or petechial in nature. The meningococcal skin lesion, however, is usually tender and comes on rapidly in comparison to Rickettsial rash occurring four days after onset^{1,2}. Other major Rickettsial diseases should include endemic typhus with a positive OX-19 titer and a truncal macular rash on the chest, shoulders, axillary folds and arms, as compared to epidemic typhus which also has an elevated OX-19 titer, but is generally a more severe disease. Q fever is classically a pneumonitis secondary to inhalation of infected dust and feces and has a negative serologic titer. It is in general a difficult diagnosis to make. Rickettsialpox is similar in that it has negative serum titers but may be confused with chickenpox because of the generalized macular, papular and petechial rash which scabs over. Coxsackie virus, Group A, may cause an unusual picture of hand, foot and mouth disease with a petechial eruption, and at the same time the so-called hemolytic uremic syndrome. Other diagnoses that may or may not be considered include systemic lupus, viral illness, idiopathic thrombocytopenia purpura, leucic disease, serum sickness, Wiskott-Aldrich syndrome and Henoch-Schonlein purpura.

Hematologic abnormalities have been described previously with thrombocytopenia, hypofibrinogenemia and decreased factors two, seven and ten^{4,5,6,7}. As early as 1964 Trigg speculated that the previously described vasculitis resulted in intravas-

cular coagulation, thrombosis and extravasation of plasma and red blood cells⁶. This resulted in a possible access of thromboplastin and plasminogen into the circulation causing fibrinogen consumption. The importance of a hematologic abnormality is intensified when one considers a ten-fold increase in mortality seen in Rocky Mountain spotted fever in patients with platelet counts of less than 25,000. Since that time much work has been done on the coagulation process and this deserves a brief review as to how it may concern Rocky Mountain spotted fever. The accepted sequence of hemostasis is divided into the vascular phase associated with tissue injury followed by extravasation of blood, increased tissue pressure and ADP release. This could easily begin with a vasculitis.

Next is the platelet phase with adhesion, aggregation and finally platelet thrombus. The coagulation phase follows with the activation of the intrinsic and extrinsic pathway down to retracted fibrin⁸. This in turn stimulates the plasminogen system to form plasmin which if unbound attacks fibrin forming degradation products. This of course, in the normal hemostatic mechanism, will not affect the clotting process. In the presence of a vasculitis this mechanism could be disrupted giving a picture similar to that described as the defibrination syndrome. This usually has two systems: first, disseminated intravascular coagulation seen in shock and sepsis causing gradual depletion of platelets, factors five, eight, fibrinogen, and prothrombin and a secondary activation of the plasminogen complex. The second system is that of the rare primary fibrinolysis which occurs in certain circumstances resulting in activation of the plasminogen system⁸. Here total binding of the antiplasmins results in hyperplasminemia and subsequent interference by fibrin and fibrin-

ogen split products D & E of long chain polymer formation after thrombin digestion of fibrinogen and subsequent inhibition of proper clot formation giving the hemorrhagic diathesis⁹. These fibrin split products also have definite antithrombin, platelet and thromboplastin activity⁹. Recent studies show that through the Hageman factor, the plasminogen system may actually activate the complement cascade and at the same time the kininogen systems facilitating chemotaxis¹⁰. This theory could show an even closer relationship between the normal inflammation process and hemostasis.

Harker and Slitcher recently summarized platelet and fibrinogen consumption in 104 patients with consumptive coagulopathy and found those disorders to be in three major areas:

1. Primary platelet destruction as seen in idiopathic thrombocytopenic purpura, prosthetic heart valves, hemolytic uremic syndrome and vasculitis.
2. Primary fibrinogen destruction receiving urokinase infusion.
3. Combined platelet and fibrinogen consumption as seen in neoplasia sepsis, venous thrombotic disease, surgical disease and obstetric defibrination. Heparin therapy prolonged fibrinogen and platelet survival with venous thrombotic disease and sepsis, but had no effect on the selective platelet destruction as seen in a vasculitis. Similarly steroids only helped the primary platelet destruction¹¹. When remembering that Trigg postulated that Rocky Mountain spotted fever was a vasculitis with thrombosis, does not this at least present a therapeutic dilemma? Is the bleeding secondary to the intrinsic vasculitis or secondary to a consumptive coagulopathy? One can only speculate that a patient with

COAGULATION DEFECTS IN ROCKY MOUNTAIN SPOTTED FEVER

DRIGGERS

Rocky Mountain spotted fever has a primary vasculitis and may have either primary platelet or combined fibrinogen and platelet destruction. This may be further confused by near normal laboratory levels maintained by compensatory mechanisms or a masquerade of disseminating intravascular coagulation caused by hepatic insufficiency and secondary prolonged prothrombin times, thrombocytopenia, hypofibrinogenemia and circulating fibrin split products not cleared by the reticuloendothelial system. In any event with a knowledge of the hemostatic and pathologic processes one must approach tick borne typhus with hemorrhagic manifestations aggressively.

Treatment: Treatment is generally directed toward the patient with Rocky Mountain spotted fever with 1) antibiotics, and 2) support for the various complications. The two drugs of choice are tetracycline in the dose of 25 mg per kilogram per day or chloramphenicol in the dose of 50 to 100 mg per kilogram per day with enough literature to support each with the following exceptions:

1. In a young child, one must weigh dental staining seen in tetracycline versus the various hematologic abnormalities seen with chloramphenicol.
2. If the patient is able to take oral medications, oral tetracycline is probably preferred.
3. Intravenous chloramphenicol can be used in extremely ill patients if the serum iron and total iron binding capacity are followed closely.

In general antibiotics should be stopped once the patient has become afebrile for 48 hours^{1,2}. Supportive care should be directed at the hypoproteinemia and subsequent edema, pneumonitis and/or pulmonary edema secondary to the vasculitis, hemato-

logic manifestations already discussed and pressure ulcers which are a result of the ischemia secondary to local pressure and the vasculitis^{1,2}.

Prevention: Prevention is a highly debatable subject when one considers the following: One study showed that 5.7% of all ticks in the Virginia area are carriers of the Rickettsiae which cause Rocky Mountain spotted fever^{1,3}. Spraying, dusting and personal inspection is important but this will not help in the outpatient clinic when confronted with an imbedded tick. Burning, gasoline or whiskey have all been suggested but agonal regurgitation may occur with these procedures infecting the wound more than by simple removal by traction.

Summary

The case report of a severely ill patient with Rocky Mountain spotted fever with thrombocytopenia was presented. After a brief clinical summary of this disease, speculation as to the cause-effect relationship between clinical purpura and coagulation defects was made leaving the ultimate decision to the physician's judgment.

References

1. PETERS, ALLEN H.: Tick Borne Typhus (Rocky Mountain Spotted Fever). JAMA 216:1003
2. JAMA News, April 1973
3. ROTHENBERG, RICHARD L.: Rocky Mountain Spotted Fever in Virginia: Clinical and Epidemiologic Features. Journal of Medical Entomology Vol VII, No. 6:663
4. MOON, JOHN H., et al: Pathological Conference. Virginia Medical Monthly Vol 98, May 1971
5. HAZARD, G. W., et al: Rocky Mountain Spotted Fever in the Eastern United States: 13 Cases from the Cape Cod Area of Massachusetts. New Engl. J. of Medicine 280:57 thru 61, 1969
6. ADKIN, M. D., et al: Case Report of (Cape Cod) Rocky Mountain Spotted Fever with Multiple Coagulation Disturbances. Pediatrics 36:627-632, 1965
7. TRIGG, J. W.: Hypofibrinogenemia in Rocky Mountain Spotted Fever, New Engl. J. of Medicine 270:1042, 1964
8. WINTROBE, M. M., T. C. VIPHALL: Disorders of Blood Coagulation, Harrison's Principles of Internal Medicine p 101652, 6th Edition Textbook of Internal Medicine p 925,
9. BAUM, SHELDON: Coagulation Disorders in Pregnancy, Pathophysiology and Treatment. J. of American Osteopathic Association 71:1055
10. RUDY, S., et al: The Complement System of Man. New Engl. J. of Medicine 287:489
11. HARKER, L. A., et al: Platelet and Fibrinogen Consumption in Man. New Engl. J. of Medicine 287:999
12. WOODWARD, T. G., et al: Rocky Mountain Spotted Fever. Harrison's Textbook of Internal Medicine p 925, 6th Edition
13. CLIFFORD, C. M., et al: Test on Ticks and Wild Birds Collected in the Eastern United States for Rickettsia and Viruses. American J. of Tropical Medicine in Hygiene 18:1057

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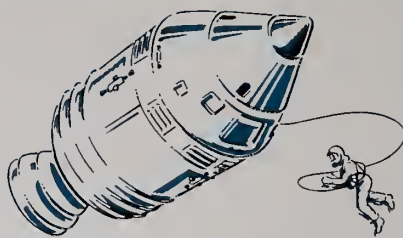
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Indications: SYNTHROID (sodium levothyroxine) is specific replacement therapy for diminished or absent thyroid function resulting from primary or secondary atrophy of the gland, congenital defect, surgery, excessive radiation, or antithyroid drugs. Indications for SYNTHROID (sodium levothyroxine) **Tablets** include myxedema, hypothyroidism without myxedema, hypothyroidism in pregnancy, pediatric and geriatric hypothyroidism, hypopituitary hypothyroidism, simple (nontoxic) goiter, and reproductive disorders associated with hypothyroidism. SYNTHROID (sodium levothyroxine) **for Injection** is indicated for intravenous use in myxedematous coma and other thyroid dysfunctions where rapid replacement of the hormone is required. The injection is also indicated for intramuscular use in cases where the oral route is suspect or contraindicated due to existing conditions or to absorption defects, and when a rapid onset of effect is not desired.

Precautions: As with other thyroid preparations, an overdose of SYNTHROID (sodium levothyroxine) may cause diarrhea or cramps, nervousness, tremors, tachycardia, vomiting and continued weight loss. These effects may begin after four or five days or may not become apparent for one to three weeks. Patients receiving the drug should be observed closely for signs of thyrotoxicosis. If indications of overdose appear, discontinue medication for 2-6 days, then resume at a lower dosage level. In patients with diabetes mellitus, careful observations should be made for changes in insulin or other antidiabetic drug dosage requirements. If hypothyroidism is accompanied by adrenal insufficiency, such as Addison's Disease (chronic adrenocortical insufficiency), Simmonds's Disease (panhypopituitarism) or Cushing's syndrome (hyperadrenalism), these dysfunctions must be corrected prior to and during SYNTHROID (sodium levothyroxine) administration. The drug

should be administered with caution to patients with cardiovascular disease; development of chest pains or other aggravations of cardiovascular disease requires a reduction in dosage.

Contraindications: Thyrotoxicosis, acute myocardial infarction. **Side effects:** The effects of SYNTHROID (sodium levothyroxine) therapy are slow in being manifested. Side effects, when they occur, are secondary to increased rates of basal metabolism; sweating, heart palpitations with or without pain, leg cramps, and weight loss. Diarrhea, vomiting, and nervousness have also been observed. Myxedematous patients with heart disease have died from abrupt increases in dosage of thyroid drugs. Careful observation of the patient during the beginning of any thyroid therapy will alert the physician to any untoward effects.

It has been shown that *Synthroid* (T₄) converts to T₃ at the cellular level to supply metabolic needs.^{1,2}

1 *Synthroid* is T₄.

2 Because T₄ converts to T₃ at the cellular level, it provides full thyroid replacement at maintenance doses.^{1,2}

3 T₄ hormone content is controlled by chemical assay.

4 *Synthroid* is assayed chemically; no biologic test is necessary to measure potency.

5 *Synthroid* provides predictable results when used with current thyroid function tests.

6 *Synthroid* is the most prescribed brand name of thyroid in the U.S. and Canada.

7 Sodium levothyroxine in *Synthroid* tablets is chemically pure. It does not contain any animal gland parts.

8 When stored properly, *Synthroid* has a longer shelf life than desiccated thyroids.

9 On a daily basis, *Synthroid* is cost competitive with other thyroid products.

The smooth road to
thyroid replacement therapy.

Synthroid[®]
(sodium levothyroxine)

In most cases with side effects, a reduction of dosage followed by a more gradual adjustment upward will result in a more accurate indication of the patient's dosage requirements without the appearance of side effects.

Dosage and Administration: The activity of a 0.1 mg. SYNTHROID (sodium levothyroxine) TABLET is equivalent to approximately one grain thyroid, U.S.P. Administer SYNTHROID tablets as a single daily dose. In hypothyroidism without myxedema, the usual initial adult dose is 0.1 mg. daily, and may be increased by 0.1 mg. every 30 days until proper metabolic balance is attained. Clinical evaluation should be made monthly and PBI measurements about every 90 days. Final maintenance dosage will usually range from 0.2-0.4 mg. daily. In adult myxedema, starting dose should be 0.025 mg. daily. The

dose may be increased to 0.05 mg. after two weeks and to 0.1 mg. at the end of a second two weeks. The daily dose may be further increased at two-month intervals by 0.1 mg. until the optimum maintenance dose is reached (0.1-1.0 mg. daily).

Supplied: Tablets: 0.025 mg., 0.05 mg., 0.1 mg., 0.15 mg., 0.2 mg., 0.3 mg., 0.5 mg., scored and color-coded, in bottles of 100, 500, and 1000. Injection: 500 mcg. lyophilized active ingredient and 10 mg. of Mannitol, U.S.P., in 10 ml. single-dose vial, with 5 ml. vial of Sodium Chloride Injection, U.S.P., as a diluent. SYNTHROID (sodium levothyroxine) **for Injection** may be administered intravenously utilizing 200-400 mcg. of a solution containing 100 mcg. per ml. If significant improvement is not shown the following day, a repeat injection of 100-200 mcg. may be given.

1. Braverman, L. E., Ingbar, S. H., and Sterling, K.: Conversion of Thyroxine (T₄) to Triiodothyronine (T₃) in Athyreotic Human Subjects, J. Clin. Invest. 49:855-64, 1970.

2. Surks, M. I., Schadow, A. R., and Oppenheimer, J. H.: A New Radioimmunoassay for Plasma L-Triiodothyronine: Measurements in Thyroid Disease and in Patients Maintained on Hormonal Replacement. J. Clin. Invest. 51:3104-13, 1972.

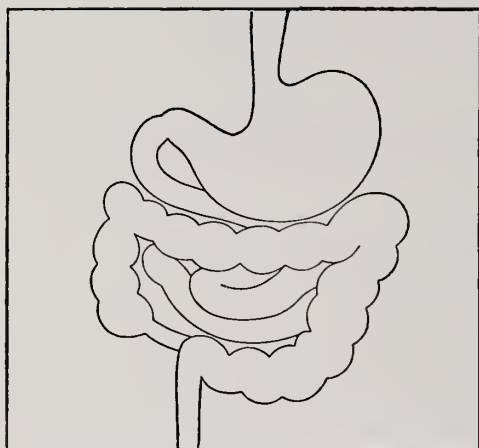


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Sidonna can calm GI spasm...control anxiety...and release entrapped GI gas from the system.

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Sidonna®

Each scored tablet contains: Specially activated simethicone 25 mg.; hyoscyamine sulfate 0.1037 mg., atropine sulfate 0.0194 mg., hyoscine hydrobromide 0.0065 mg. (equivalent to belladonna alkaloids [as bases] 0.1049 mg.) and butabarbital sodium N.F. 16 mg. (Warning: May be habit forming.)

can do more

Contraindications: Anticholinergics should not be used in patients with glaucoma, known prostatic hypertrophy, or pyloric obstruction. Urinary retention may indicate the presence of prostatic hypertrophy. If it occurs, the dose should be reduced or the drug withdrawn. Also contraindicated in patients with known hypersensitivity to one of the components.
Side Effects: Dryness of the mouth, blurred vision, dysuria, skin rash, constipation or drowsiness may occur.

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SPECIAL ARTICLE

Clifton R. Gruver, M.D.



President Medical Society of the District of Columbia

The 107th President of the Medical Society of the District of Columbia, Dr. Clifton R. Gruver, assumed his new office on January 1, 1974.

Dr. Gruver, a native of Washington, D.C., was born March 12, 1922. He attended D.C. public schools and received his B.A. and M.D. degrees from the University of Virginia. A member of the U.S. Naval Reserve from 1945-1948, Dr. Gruver served his internship in the U.S. Naval Hospital, Pensacola, Florida (with the rank of Lieutenant j.g.) and was a medical officer at various other posts. Dr. Gruver received his graduate training at Georgetown University. He was Junior Assistant Resident in Medicine from 1948-1949; Resident in Medicine at D.C. General Hospital from 1949-1950; and Fellow in Cardiology at Georgetown University Hospital from 1950-1951. He is certified by the American Board of Internal Medicine. In 1951 Dr. Gruver commenced private practice, which he has maintained to the present.

He has been on the faculty of Georgetown University Hospital from 1951 to the present. Teaching positions held include Instructor in Medicine—Georgetown University Hospital, 1951-1956; Clinical Assistant Professor of Medicine—Georgetown University Hospital, 1956-1962; Clinical Associate Professor of Medicine—Georgetown University Hospital, 1962-1970; and Clinical Professor of Medicine—Georgetown University Hospital, 1970-present.

Dr. Gruver was on the Clinical Advisory Committee of Georgetown University from 1961 to the present and was on the Affirmative Action Committee of that university from 1972 to the present. He is an active member of the attending medical staff (executive and teaching) of Doctors Hospital; an associate member of the attending medical staff of Sibley Memorial Hospital; and has courtesy privileges in internal medicine at Arlington Hospital, Washington Hospital Center and The George Washington University Hospital.

A member of the Medical Society of D.C. since June 23, 1951, Dr. Gruver has served as Chairman of the Society's Public Health Committee, 1956-1958; Chairman of the Medical Service Committee, 1965-1966; Chairman, Committee of Environmental Health, D.C. Medical Society, 1969-1971; and as alternate delegate to the American Medical Association from the District of Columbia Medical Society, 1962-1966.

Dr. Gruver is active in a number of other professional organizations including the American Medical Association; the University of Virginia Alumni Association (serving as the university's representative in medicine for the District of Columbia area); the American Society of Internal Medicine; Chairman, Medical Services, D.C. Society of Internal Medicine; past-president, Louis Mackall Society; member of the American College of Physicians; the Washington Heart Association; and he has served on the Visiting Nurses Advisory Board. He also serves as Chief Medical Examiner of Metropolitan Washington for the New England Mutual Life Insurance Company.

Long active in community affairs, Dr. Gruver was a member of the Metropolitan Welfare Council for two years; Co-Chairman of the Asian Influenza Committee to the Commissioner, D.C. Government, 1957; member, the Board of Appeals and Review, D.C. Commissioners, D.C. Government; and a member of the Washington Board of Trade.

Awards for distinguished service were presented to Dr. Gruver by the American Medical Association (The Physicians Recognition Award, 1970-73/1972-75) and by Georgetown University (The Vicennial Medical Award, 1950-70).

Dr. Gruver married Carolyn Stratton of Clifton Forge, Virginia, in 1945. The Gruvers, who reside in Bethesda, Maryland, have three children (Nancy, Lynne and Clifton, Jr.) and one grandchild.

In his leisure time, Dr. Gruver enjoys golf, fishing, bridge and is a music-lover.

A dignified and tactful man, Dr. Gruver has demonstrated the energy and community interest necessary for an effective President. The Medical Society of D.C. is fortunate to have a president with Dr. Gruver's capabilities.



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Editor Medical Annals of the District of Columbia

The Executive Board of the Medical Society of the District of Columbia takes great pleasure in announcing the appointment of Dr. Robert B. W. Smith as Editor of the MEDICAL ANNALS OF THE DISTRICT OF COLUMBIA effective January 1, 1974.

Born in Recife, Pernambuco, Brazil, he received his M.D. degree from Columbia University College of Physicians and Surgeons. He served his internship at Denver General Hospital and his residency at Walter Reed Army Hospital here.

Commissioned a First Lieutenant in the U.S. Air Force in 1949, Dr. Smith has had a most distinguished military career. He served as Chairman of the Department of Medicine at the Malcolm Grow U.S. Air Force Medical Center at Andrews Air Force Base here, and then as Deputy Director of Professional Services in the Office of the Surgeon General, U.S. Air Force. At the time of his retirement from the military in 1971 he held the rank of Colonel and the position of Chief Professional Consultant and Chief, Consultants Division, Office of the Surgeon General, U.S. Air Force.

He is currently an Associate Clinical Professor of Medicine at George Washington University School of Medicine. He is also Senior Attending Physician at the Washington Hospital Center and on the attending staff at Doctors Hospital.

An active member of the Medical Society of the District of Columbia, Dr. Smith also holds membership in the American Medical Association, the American Thoracic Society and the Society of Air Force Physicians. He is a Fellow of the American College of Physicians, of which he served as Governor for the Air Force from 1968 to 1971, and he is also a Fellow in the American College of Chest Physicians.

Author of a number of scientific articles, Dr. Smith's literary talents were employed in the writing of a book on the ornithology of Japan. His interest in ornithology has led to the collection of a large ornithology library containing many rare volumes. He has a weekend home/studio on Maryland's eastern shore, where he pursues his further interest in painting the birds of his studies.

He is married to the former Etsuko Yoshimura of Tokyo, Japan. They reside in Bethesda, Maryland with their four sons, John Rockwell, 20, Bruce Robert, 17, Peter Francis, 14, and Richard Warfield, 4.

What's on your patient's face...

may be more important than his chief complaint

Patient PT.* seen on 3/29/67 shows typical lesions of moderately severe keratoses. Note residual scarring on ridge of nose from previous cryosurgical and electrosurgical procedures.



Patient PT.* seen on 6/12/67, seven weeks after discontinuation of 5% FU cream. Reaction has subsided. Residual scarring not seen except that due to prior surgery. Inflammation has cleared and face is clear of keratotic lesions.

*Data on file, Hoffmann-La Roche Inc., Nutley, N.J



The lesions on his face are solar/actinic—so-called "senile" keratoses... and they may be premalignant.

Solar, actinic or senile keratoses

These lesions may be called by several names, but they usually can be identified by the following characteristics. The typical lesion is flat or slightly elevated, of a brownish or reddish color, papular, dry, rough, adherent and sharply defined. They commonly occur as multiple lesions, chiefly on the exposed portions of the skin.

Sequence of therapy—selectivity of response

After several days of therapy with Efudex® (fluorouracil), erythema may begin to appear in the area of the lesions; this reaction usually reaches its height of unsightliness and discomfort within two weeks, declining after discontinuation of therapy. This reaction occurs in affected areas. Since the response is so predictable, lesions that do not respond should be biopsied.

Acceptable results

Treatment with Efudex provides highly favorable cosmetic results. Incidence of scarring is low. This is particularly important with multiple facial lesions. Efudex should be applied with care near the eyes, nose and mouth.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Multiple actinic or solar keratoses.

Contraindications: Patients with known hypersensitivity to any of its components.

Warnings: If occlusive dressing used, may increase inflammatory reactions in adjacent normal skin. Avoid prolonged exposure to ultraviolet rays. Safe use in pregnancy not established.

Precautions: If applied with fingers, wash hands immediately. Apply with care near eyes, nose and mouth. Lesions failing to respond or recurring should be biopsied.

Adverse Reactions: Local—pain, pruritus, hyperpigmentation and burning at application site most frequent; also dermatitis, scarring, soreness and tenderness. Also reported—insomnia, stomatitis, suppuration, scaling, swelling, irritability, medicinal taste, photosensitivity, lacrimation, leukocytosis, thrombocytopenia, toxic granulation and eosinophilia.

Dosage and Administration: Apply sufficient quantity to cover lesion twice daily with nonmetal applicator or suitable glove. Usual duration of therapy is 2 to 4 weeks.

How Supplied: Solution, 10-ml drop dispensers—containing 2% or 5% fluorouracil on a weight/weight basis, compounded with propylene glycol, tris(hydroxymethyl)-aminomethane, hydroxypropyl cellulose, parabens (methyl and propyl) and disodium edetate.

Cream, 25-Gm tubes—containing 5% fluorouracil in a vanishing cream base consisting of white petrolatum, stearyl alcohol, propylene glycol, polysorbate 60 and parabens (methyl and propyl).



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110

This patient's lesions were resolved with

Efudex® fluorouracil/Roche®

5% cream/solution...a Roche exclusive

THE VIEW BOX

(from page 14)

DIAGNOSIS: Paraesophageal foregut cyst containing cartilage and smooth muscle

Note the paraesophageal location of the mass in the posterior mediastinum displacing the esophagus forward without significantly indenting the wall of the esophagus. There are no bony abnormalities.

The differential diagnosis includes neurogenic tumors, including neuroenteric cyst and foregut cyst as the most likely possibilities.

Foregut cysts are congenital in origin. They can be in the wall of the esophagus and, if in the lower one-third, are often lined with gastric epithelium. Cysts that are paraesophageal in location are often lined by respiratory epithelium. Not infrequently this lesion is associated with malformations in other organs and, indeed, cardiac work-up of this patient, including cardiac catheterization, revealed a bicuspid aortic valve.

*Edited by Gunther J. Augustin, M.D.
Senior Attending Radiologist, Washington
Hospital Center, Washington, D.C.*

ECG DIAGNOSIS

(from page 8)

INTERPRETATION:

1. Frequent nonconducted atrial premature beats with ventricular escape beats.
2. First degree A-V block.

The top strip begins with six beats of sinus rhythm. The PR interval is approximately 0.22 seconds, though it is difficult to measure since the P wave begins in the preceding T wave. The ST segment of the sixth beat is deformed by the P wave of an atrial premature beat. This is not followed by a QRS complex ("non-conducted") because the ventricles are still in their refractory period following the sixth beat. Similar very early atrial premature beats appear in the subsequent strips. When they occur every other beat, the effective ventricular rate is only 50 per minute. The pause following these premature beats is long enough for a ventricular focus to discharge as escape beats. These escape beats appear as the third and seventh beat in the third strip and beats number two, four, six, seven, and nine in the third strip.

Edited by Robert R. Montgomery, M.D.

POST GRADUATE EDUCATION

THE USE OF LIVER FUNCTION TESTS

Stuart H. Danovitch, M.D.

Few problems perplex the physician as frequently as that of the jaundiced patient. The dilemma always portrays itself by asking the two questions: whether surgery is indicated, and what is the diagnosis.

Whereas the history and physical examination can very often yield important information, one looks to the liver function studies to confirm the presence of an abnormality as well as to point toward the cause and answer the question of the need for surgery.

Routine blood work and urine seldom yield helpful information, although the presence of bile in the urine certainly excludes those patients whose jaundice is characterized by retention of indirect or unconjugated bilirubin.

Because no single liver function study is so discriminating as to be a reliable indicator of the disease process at hand, we run a "profile" or "battery" to help solve the problems. The exception to this is detection of hepatitis B antigen, which implies a causal relation between the virus and jaundice. A serum bilirubin determination, apart from its confirmation of the presence of jaundice, adds little diagnostic information, unless the partition is 90% in one direction or the other. Serum transaminase activities, on the other hand, offer certain discriminatory value when in excess of 300-400 units. Commonly only viral hepatitis, drug or toxic hepatitis, and acute circulatory changes such as shock or acute congestive failure account for such changes in magnitude.

Obstructive jaundice as a cause of transaminase levels in excess of 300 units account for no more than 1% of such measurements. Serum alkaline phosphatase activity has been said to be helpful in the distinction of extrahepatic from intrahepatic cholestasis when its activity is extraordinarily high. However, practical experience indicates that normal or minimally elevated ($1\frac{1}{2}$ to 2 times normal) serum alkaline phosphatase activity serves a far more discriminatory function by minimizing the likelihood of obstruction, especially that due to malignancy, than an elevated serum alkaline phosphatase discriminates in favor of

obstruction. The commonly occurring abnormalities in serum protein electrophoresis of low albumin concentration and high gamma globulin concentration tend to bespeak chronic as opposed to acute liver disease, and these abnormalities are often associated with prolongation of prothrombin time and other clotting studies. I have found little usefulness in the determination of serum lactic acid dehydrogenase (LDH) activity since so many things influence this enzyme. Similarly, determination of plasma BSP retention after 45 minutes is useful in very limited circumstances. Its routine use is considered by some to be deplorable because of the attendant hazards, and its overall sensitivity again precludes any diagnostic specificity. Others maintain that the presence of a direct-reading serum bilirubin concentration in excess of 0.2 mg/100 ml correlates with BSP retention and hence makes its determination pointless in that circumstance.

A plethora of other less commonly available serum studies reflecting liver function are available in many laboratories. Their employment does not, however, appear to add to the discriminate function of tests outlined above, with the exception of α -fetoprotein in the diagnosis of hepatoma and the antimitochondrial (cytoplasmic?) antibody studies in primary biliary cirrhosis.

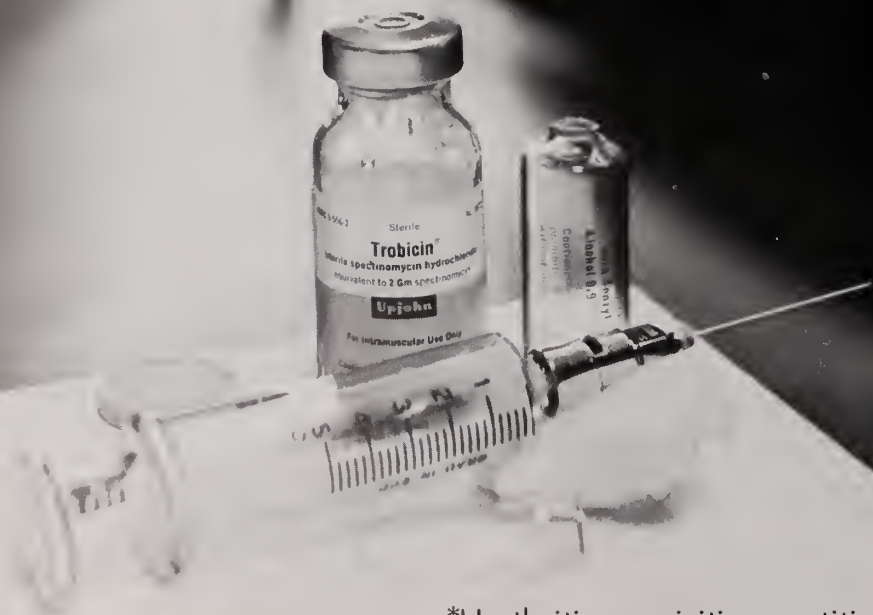
Further help can be gleaned from radionuclide scanning of the liver, particularly with selectivity of the isotopes used. In patients with extrahepatic obstruction, ^{131}I rose bengal may be preferable to the commonly used technetium-99m sulfa-colloid scans, while in patients suspected of primary or metastatic carcinoma, gallium-67 citrate scanning may be useful.

Finally, that most diagnostic, usually, of all liver function studies is the liver biopsy and should be utilized appropriately when laboratory tests do not provide a satisfactory answer with a high (90%) degree of certainty, and when safety permits.

acute gonorrhea

This patient
just received
an effective, private,
physician-controlled
treatment.

It took just one short visit



*Urethritis, cervicitis, proctitis when due
to susceptible strains of *N. gonorrhoeae*

Trobicin—The advantage of injectable therapy.

Once Trobicin is injected, treatment is usually complete; there can be no problems with patients sharing, skimping, skipping or forgetting medication.

Trobicin—The aspect of privacy.

There are no prescriptions to fill, no capsules to take.

Neither family, friends nor co-workers need know or suspect the patient's problem.

Trobicin—Indication and dosage.

Spectinomycin is indicated only for use in acute urethritis and proctitis in the male and acute cervicitis and/or proctitis in the female when due to susceptible strains of *N. gonorrhoeae*.

The usual dosage for Trobicin in adult males is 2 grams intramuscularly¹; 4 grams intramuscularly in females.

Trobicin—Not effective for syphilis.

Trobicin is not effective for any stage of syphilis. Trobicin may mask or delay the symptoms of incubating syphilis. If concurrent syphilis is suspected, follow the patient serologically for at least 3 months. Patients with syphilis should receive adequate specific anti-syphilitic therapy with an appropriate antibiotic.

Trobicin is contraindicated in patients previously found hypersensitive to it.

Intramuscular

...and **Trobicin**[®] 2 gm and 4 gm vials sterile spectinomycin hydrochloride

Sterile Trobicin

*Sterile Trobicin (spectinomycin hydrochloride)
—For Intramuscular Injection:*

2 gm vials containing 5 ml when reconstituted with diluent.

4 gm vials containing 10 ml when reconstituted with diluent.

An aminocyclitol antibiotic active *in vitro* against most strains of *Neisseria gonorrhoeae* (MIC 7.5 to 20 mcg/ml). Definitive *in vitro* studies have shown no cross resistance of *N. gonorrhoeae* between spectinomycin and penicillin.

Indications: Acute gonorrheal urethritis and proctitis in the male and acute gonorrheal cervicitis and proctitis in the female when due to susceptible strains of *N. gonorrhoeae*.

Contraindications: Contraindicated in patients previously found hypersensitive to spectinomycin.

Warnings: Not indicated for the treatment of syphilis. Antibiotics used to treat gonorrhea may mask or delay the symptoms of incubating syphilis. Patients should be carefully examined and monthly serological follow-up for at least 3 months should be instituted if the diagnosis of

syphilis is suspected.

Safety for use in infants, children and pregnant women has not been established.

Precautions: The usual precautions should be observed with atopic individuals. Clinical effectiveness should be monitored to detect evidence of development of resistance by *N. gonorrhoeae*.

Adverse reactions: The following reactions were observed during the single-dose clinical trials: soreness at the injection site, urticaria, dizziness, nausea, chills, fever and insomnia. During multiple-dose subchronic tolerance studies in normal human volunteers, the following were noted: a decrease in hemoglobin, hematocrit and creatinine clearance; elevation of alkaline phosphatase, BUN and SGPT. In single- and multiple-dose studies in normal volunteers, a reduction in urine output was noted. Extensive renal function studies demonstrated no consistent changes indicative of renal toxicity.

Dosage and administration: Keep at 25° C and use within 24 hours after reconstitution with diluent.

Male—Inject 5 ml intramuscularly for a 2 gram dose. Patients with gonorrheal proctitis and patients being re-treated after failure of previous antibiotic therapy should receive 4 grams (10 ml). In geographic areas where antibiotic resistance is known to be prevalent, initial treatment with 4 grams (10 ml) intramuscularly is preferred.

Female—Inject 10 ml intramuscularly for a 4 gram dose.

How supplied: Vials, 2 and 4 grams—with ampoule of Bacteriostatic Water for Injection with Benzyl Alcohol 0.9% w/v. Reconstitution yields 5 and 10 ml respectively with a concentration of 400 mg spectinomycin per ml (as the hydrochloride). For intramuscular use only. **Susceptibility Powder**—for testing *in vitro* susceptibility of *N. gonorrhoeae*.

Caution: Federal law prohibits dispensing without prescription.

For additional product information see your Upjohn representative or consult the package insert.

Upjohn

The Upjohn Company, Kalamazoo, Michigan 49001

MED B-5-S (MBR-1)

¹For patients with gonorrheal proctitis and for patients in geographic areas where antibiotic resistance is known to be prevalent, initial treatment with 4 grams is preferred.

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CholoXin[®]
(sodium dextrothyroxine)

Once-a-day dosage.

See reverse side for full prescribing
information and dosage schedule.



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The Lipid-Lowering Agent with Once-A-Day Dosage

Four strengths . . . 1, 2, 4, and 6 mg. . . are available making the scored tablet regimen a flexible dosage system. And, for most patients, CHOLOXIN tablets offer once-a-day dosage.

CHOLOXIN® (sodium dextrothyroxine) Single-Tablet-A-Day Dosage Schedules

See prescribing information in package insert reproduced below.

	Starting Dosage	Increased by Increments of	Usual Maintenance	Maximal Recommended
Adult Hypercholesterolemic	1.0-2.0 mg.	monthly 1.0-2.0 mg.	4.0-8.0 mg.	4.0-8.0 mg.
Pediatric Hypercholesterolemic	0.05 mg./kg. body weight	monthly 0.05 mg./kg.	0.1 mg./kg. body weight	4.0 mg.
Hypothyroid Cardiac Patients	0.5-1.0 mg.	monthly 1.0 mg.	4.0 mg.	4.0 mg.

Choloxin® (sodium dextrothyroxine)

Description

CHOLOXIN (sodium dextrothyroxine) is the sodium salt of the dextrorotatory isomer of thyroxine. It is chemically described as D-3,5,3',5'-tetraiodothyronine sodium salt.

Actions

The predominant effect of CHOLOXIN (sodium dextrothyroxine) is the reduction of serum cholesterol levels in hyperlipidemic patients. Beta lipoprotein and triglyceride fractions may also be reduced from previously elevated levels.

Most of the available evidence indicates that CHOLOXIN stimulates the liver to increase catabolism and excretion of cholesterol and its degradation products via the biliary route into the feces. Cholesterol synthesis is not inhibited and abnormal metabolic end-products do not accumulate in the blood.

Indications

This is not an innocuous drug. Strict attention should be paid to the indications and contraindications.

CHOLOXIN (sodium dextrothyroxine) is an antilipidemic agent used as an adjunct to diet and other measures for the reduction of elevated serum cholesterol (low density lipoproteins) in euthyroid patients with no known evidence of organic heart disease.

The drug is also indicated in the treatment of hypothyroidism in patients with cardiac disease who cannot tolerate other types of thyroid medication. Before prescribing, note the following: Results from a randomized clinical study have indicated a possible adverse effect when CHOLOXIN is administered to a patient receiving a digitalis preparation. There may be an additive effect. This additive effect may possibly stimulate the myocardium excessively in patients with significant myocardial impairment. CHOLOXIN dosage should not exceed 4 mg per day when the patient is receiving a digitalis preparation concomitantly. Careful monitoring of the total effect of both drugs is important.

It has not been established whether the drug-induced lowering of serum cholesterol or lipid levels has a detrimental, beneficial, or no effect on the morbidity or mortality due to atherosclerosis or coronary heart disease. Several years will be required before current investigations will yield an answer to this question.

Contraindications

The administration of CHOLOXIN (sodium dextrothyroxine) to euthyroid patients with one or more of the following conditions is contraindicated:

1. Known organic heart disease, including angina pectoris; history of myocardial infarction; cardiac arrhythmia or tachycardia, either active or in patients with demonstrated propensity for arrhythmias; rheumatic heart disease; history of congestive heart failure; and decompensated or borderline compensated cardiac status.
2. Hypertensive states (other than

3. Advanced liver or kidney disease.
4. Pregnancy.
5. Nursing mothers.
6. History of iodism.

Warnings

CHOLOXIN (sodium dextrothyroxine) may potentiate the effects of anticoagulants on prothrombin time. Reductions of anticoagulant dosage by as much as 30% have been required in some patients. Consequently, the dosage of anticoagulants should be reduced by one-third upon initiation of CHOLOXIN therapy and the dosage subsequently readjusted on the basis of prothrombin time. The prothrombin time of patients receiving anticoagulant therapy concomitantly with CHOLOXIN therapy should be observed as frequently as necessary, but at least weekly, during the first few weeks of treatment.

In the surgical patient, it is wise to consider withdrawal of the drug two weeks prior to surgery if the use of anticoagulants during surgery is contemplated.

When CHOLOXIN is used as thyroid replacement therapy in hypothyroid patients with concomitant coronary artery disease (especially those with a history of angina pectoris or myocardial infarction) or other cardiac disease, treatment should be initiated with care. Special consideration of the dosage schedule of CHOLOXIN is required. This drug may increase the oxygen requirements of the myocardium, especially at high dosage levels. Treated subjects with coronary artery disease must be seen at frequent intervals. If aggravation of angina or increased myocardial ischemia, cardiac failure, or clinically significant arrhythmia develops during the treatment of hypothyroid patients, the dosage should be reduced or the drug discontinued.

Special consideration must be given to the dosage of other thyroid medications used concomitantly with CHOLOXIN. As with all thyroactive drugs, hypothyroid patients are more sensitive to a given dose of CHOLOXIN than euthyroid patients.

Epinephrine injection in patients with coronary artery disease may precipitate an episode of coronary insufficiency. This condition may be enhanced in patients receiving thyroid analogues. These phenomena should be kept in mind when catecholamine injections are required in sodium dextrothyroxine-treated patients with coronary artery disease.

Since the possibility of precipitating cardiac arrhythmias during surgery may be greater in patients treated with thyroid hormones, it may be wise to discontinue CHOLOXIN in euthyroid patients at least two weeks prior to an elective operation. During emergency surgery in euthyroid patients, and in surgery in hypothyroid patients in whom it may be advisable to withdraw therapy, the patients should be carefully observed.

There are reports that sodium dextrothyroxine in diabetic patients is capable of increasing blood sugar levels with a resultant increase in requirements of insulin or oral hypoglycemic agents. Special attention should be paid to parameters necessary for good control of the diabetic state in dextrothyroxine-treated subjects and to

antidiabetic drugs. If sodium dextrothyroxine is later withdrawn from patients who had required an increase of insulin (or oral hypoglycemic agents) dosage during its administration, the dosage of antidiabetic drugs should be reduced and adjusted to maintain good control of the diabetic state.

When either or both impaired liver or kidney function are present, the advantages of CHOLOXIN therapy must be weighed against the possibility of deleterious results.

Usage in Women of Childbearing Age
Women of childbearing age with familial hypercholesterolemia or hyperlipemia should not be deprived of the use of this drug; it can be given to those patients exercising strict birth control procedures. Since pregnancy may occur despite the use of birth control procedures, administration of CHOLOXIN (sodium dextrothyroxine) to women of this age group should be undertaken only after weighing the possible risk to the fetus against the possible benefits to the mother. Teratogenic studies in two animal species have resulted in no abnormalities in the offspring.

Precautions

It is expected that patients on dextrothyroxine therapy will show greatly increased serum protein-bound-iodine levels. These increased serum PBI values are evidence of absorption and transport of the drug, and should NOT be interpreted as evidence of hypermetabolism; similarly, they may not be used for titrating the effective dose of CHOLOXIN (sodium dextrothyroxine). PBI values in the range of 10 to 25 mcg% in treated patients are common.

If signs or symptoms of iodism develop during CHOLOXIN therapy, the drug should be discontinued.

A few children with familial hypercholesterolemia have been treated with CHOLOXIN for periods of one year or longer with no adverse effects on growth. However, it is recommended that the drug be continued in patients in this age group only if a significant serum cholesterol-lowering effect is observed.

Adverse Reactions

The side effects attributed to dextrothyroxine therapy are, for the most part, due to increased metabolism, and may be minimized by following the recommended dosage schedule. Adverse effects are least commonly seen in euthyroid patients with no signs or symptoms of organic heart disease; the incidence of adverse effects is increased in hypothyroid patients, and is highest in those patients with organic heart disease superimposed on the hypothyroid state.

In the absence of known organic heart disease, some cardiac changes may be precipitated during sodium dextrothyroxine therapy. In addition to angina pectoris, arrhythmia consisting of extrasystoles, ectopic beats, or supraventricular tachycardia, ECG evidence of ischemic myocardial changes and increase in heart size have been observed. Myocardial infarctions, both fatal and non-fatal, have occurred, but these are not unexpected in untreated patients in the age groups studied. It is not known whether any of these infarcts were drug related.

Changes in clinical status that may be related to the metabolic action of the drug include the development of in-

temors, loss of weight, lid lag, sweating, flushing, hyperthermia, hair loss, diuresis, and menstrual irregularities. Gastrointestinal complaints during therapy have included dyspepsia, nausea and vomiting, constipation, diarrhea, and decrease in appetite.

Other side effects reported to be associated with CHOLOXIN (sodium dextrothyroxine) therapy include the development of headache, changes in libido (increase or decrease), hoarseness, tinnitus, dizziness, peripheral edema, malaise, tiredness, visual disturbances, psychic changes, paresthesia, muscle pain, and various bizarre subjective complaints. Skin rashes, including a few which appeared to be due to iodism, and itching have been attributed to dextrothyroxine by some investigators. Gallstones have been discovered in occasional dextrothyroxine-treated patients and cholestatic jaundice has occurred in one patient, although its relationship to CHOLOXIN therapy was not established.

In several instances, the previously existing conditions of the patient appeared to continue or progress during the administration of CHOLOXIN; a worsening of peripheral vascular disease, sensorium, exophthalmos, and retinopathy have been reported.

CHOLOXIN potentiates the effects of anticoagulants, such as warfarin or Dicumarol, on prothrombin time, thus indicating a decrease in the dosage requirements of the anticoagulants. On the other hand, dosage requirements of antidiabetic drugs have been reported to be increased during dextrothyroxine therapy (see WARNINGS section).

Dosage and Administration

For adult euthyroid hypercholesterolemic patients, the recommended maintenance dose of CHOLOXIN (sodium dextrothyroxine) is 4 to 8 mg per day. The initial daily dose should be 1 to 2 mg to be increased in 1 to 2 mg increments at intervals of not less than one month to a maximum level of 4 to 8 mg daily, if that dosage level is indicated to effect the desired lowering of serum cholesterol.

When used as partial or complete substitution therapy for levothyroxine in hypothyroid patients with cardiac disease who cannot tolerate other types of thyroid medication, the initial daily dose should be 1 mg to be increased in 1 mg increments at intervals of not less than one month to a maximum level of 4 to 8 mg daily, preferably the lower dosage. The maximum in patients receiving digitalis therapy is 4 mg.

For pediatric hypercholesterolemic patients, the recommended maintenance dose of CHOLOXIN is approximately 0.1 mg per kilogram. The initial daily dosage should be approximately 0.05 mg per kilogram to be increased in up to 0.05 mg per kilogram increments at monthly intervals. The recommended maximal dose is 4 mg daily, if that dosage is indicated to effect the desired lowering of serum cholesterol.

If new signs or symptoms of cardiac disease develop during the treatment period, the drug should be withdrawn.

How Supplied

CHOLOXIN (sodium dextrothyroxine) is supplied in prescription packages of scored 1, 2, 4, and 6 mg tablets.

IMPORTANT NOTE:

It has not been established whether the drug-induced lowering of serum cholesterol or lipid levels has a detrimental, beneficial, or no effect on the morbidity or mortality due to atherosclerosis or coronary heart disease. Several years will be required before current investigations will yield an answer to this question.



BOOK REVIEWS

Clinical Electroneurography. MARIO P. SMORTO AND JOHN V. BASMAJIAN. Price, \$16.75. Pp. 234 with illustrations. Baltimore, Md.: The Williams & Wilkins Company, 1972.

"Clinical Electroneurography" is a short but extremely precise, well-written monograph on electromyography and nerve conduction time testing. The book is well-indexed, thoroughly referenced, and its diagrams, photographs and charts are accurately and pleasingly reproduced. The great emphasis on the book is on the neuropathic diseases with only a brief section on the myopathies. In addition to the technical aspects of performing and interpreting nerve conduction times, there is an easily read physiological and clinical section. The book is of limited interest to anyone other than those dealing with clinical neurology and electrodiagnostic studies, but is highly recommended for such individuals.

HOWARD M. SILBY, M.D.

Pediatric Otolaryngology, Vol. II of Disorders of the Respiratory Tract in Children. CHARLES F. FERGUSON, M.D. AND EDWIN L. KENDIG, JR., M.D., Editors. Price, \$25.00. Pp. 572 with illustrations. Philadelphia: W. B. Saunders, 1972.

This textbook is an up-to-date book, geared to medical students, residents in pediatrics and otolaryngology. It is an excellent review for the practicing specialist. The editors skillfully selected about forty contributors, each one a top authority in his own field. Very little overlapping, and practically no contradictory opinion was found in the book. The eight sections in the textbook cover all phases of otolaryngology, including the various treatment methods and latest surgical techniques. Due to the intent and nature of the textbook, details are often omitted, and the extent of the chapters is limited, but excellent bibliography follows them. All the sections are quite good, and no detail is overlooked which would interest a pediatrician or an otolaryngologist. I enjoyed the most, the section on the laryngotracheobronchial tree and esophagus; it is the most thorough and comprehensive description, and is reaching a postgraduate level.

I recommend reading this book to my colleagues in pediatrics and otolaryngology, and it should be a must to those preparing for the boards in pediatrics and otolaryngology.

LOUIS B. BALLA, M.D., P.C.

Statistics in Small Doses. WINIFRED M. CASTLE. Price, \$9.50. Pp. 216. Baltimore, Maryland: Williams & Wilkins Publishing Co., 1972.

Since information comes to us largely in the numerical form it is essential that we understand this language. Even the case history must be related to the group which it characterizes and to the general population of which it is a part.

Lord Calvin (1894) wrote, "When you can measure what you are speaking about, and express it in numbers, you know something about it; but when you cannot measure it, when you cannot express it in numbers, your knowledge is of a meager and unsatisfactory kind: it may be the beginning of knowledge, but you have scarcely, in your thoughts, advanced to the stage of science." If Lord Calvin's observations pertain also to medicine then we shall continue to see a trend toward mathematical expression.

The text by Winifred Castle should be of interest to all physicians. If the physician is in training it will provide a help in interpreting medical knowledge, if a clinician it will provide insight into information being read daily in journals and other periodicals, and if a teacher it will be of help in preparing data for presentation. The processes presented are within the capability of the practicing physician.

This book is interesting. Fortunately its narrative is reduced to a minimum with graphic displays. If a point becomes too complex then the reader need only to turn back and review the descriptive material developing that concept. It is the type of text that one can pick up and read for a short time and gain information. It doesn't make statistics completely painless but it does reduce the anticipated bore.

JAMES R. SNYDER, M.D.

BOOK REVIEWS

Major Modalities in the Treatment of Drug Abuse. LEON BRILL AND LOUIS LIEBERMAN, Editors. Price, \$12.75. Pp. 313. New York, Behavioral Publications, 1972.

The American Heroin Empire, Power, Profits, and Politics. RICHARD KUNNES, M.D. Price, \$5.95. Pp. 215. New York: Dodd, Mead & Co., 1973.

Brill and Lieberman have edited another book in the Drug Abuse Series published by Behavior Publications. This book, like the others in the series, is a collection of separate papers covering widely varying topics in the drug abuse field. In this book some of the major figures in the field have been asked to describe their programs and share their observations. The topics covered range from methadone maintenance to religion and to street social work. Although there are useful passages in the book, the overall effect is chaotic. There is no attempt to integrate the 16 contributions of 21 authors.

Richard Kunnes has written a polemic about heroin. The book appears to be a collection of paragraphs each of which is derived from a separate index card taken from a file laboriously built up in a good library. It lacks coherence as does the Brill and Lieberman book. Although published only a year ago, Kunnes' book is oddly dated in the fast-changing heroin addiction field. He is primarily concerned with the addiction of servicemen in Vietnam and the failures of our domestic policy of heroin addiction control. Since the publication of his book we have convincing evidence that few (about 7%) of the servicemen addicted to heroin in Vietnam are still using the drug a year later in this country.¹ We also have growing evidence that the current policy combining treatment opportunities with heroin supply reduction programs are working to stem the tide of the epidemic.² Few people feel today as passionately on these points as Dr. Kunnes obviously did when he wrote the book.

Those who would like to read a coherent, readable, informative book on the problems of drug abuse are referred to *Licit and Illicit Drugs* by Edward Brecher and the Editors of Consumers Report. It is possible to quarrel with some positions taken by Brecher (for example, he also wrote before there was clear evidence of

the epidemic nature of heroin addiction and the recent downturn in addiction rates), but on balance he has made a major contribution to the field. The other general reference which will repay careful reading is the second volume of the Shafer Commission reports, *Drug Abuse in Perspective*, also published in 1973 and also authoritative and comprehensive.

ROBERT DuPONT, JR., M.D.

¹ Robins, Lee N., Ph.D., "A Follow-Up of Vietnam Drug Users." *Special Action Office Monograph Series A*, Number 1, April 1973.

² DuPont, Robert L. and Greene, Mark H., "The Dynamics of a Heroin Addiction Epidemic." *Science* Vol. 181, pp. 716-722, August 24, 1973.

The American Medical Machine. SENATOR ABRAHAM RIBICOFF WITH PAUL DANACEAU. Price, \$6.95. Pp. 212. New York: Saturday Review Press, 1972.

The American Medical Machine is really an excellent survey book of the problems, with examples of the present status of the American health, in education and training as well as delivery system. The author probably would have said non-system or cottage industry, but this only illustrates the tendency to hide good data under somewhat scare title and chapter headings which will undoubtedly lose many conservative readers. The book is well organized and has a good index.

Senator Ribicoff's personal credentials for writing such a book are impeccable. In addition, he has used many sources in the health profession as well as among educators, practitioners, clinics, researchers, administrators, and theorists.

He uses many anecdotal references. Most questionable, in my opinion, are those which give the severe medical problems of his family or the ordinary ones of his own which are so magically solved without use of VIP influence. (Wanta bet!) These illustrations are the most favorable to the status quo. Most of the others, whether anecdotal, statistical or by opinion of the proper professionals, are devastating to the

present (I paraphrase) fragmented, doctor-oriented, unresponsive, dollar and third-party governed non-system.

I think the Senator does recognize that most physicians, nurses and hospital administrators like their work, are humane, are conscientious, and are hard working. Most of the illustrations and citations show the physician, except for certain favored groups, clinics, rural doctors and health organizers and his own family doctors, as being at least somewhat taken with himself as god-like, money-grubbing, stultified, uncaring, specialized and research-oriented.

But some of his examples are so acute, so true and so sharp that they drive home the message of the book to this physician-reader-reviewer who is also an educator-administrator-practitioner combined. The author's messages are:

1. Good medical care is poorly distributed, costly and at least somewhat unresponsive to patients' criticisms. It is in need of change.
2. It is a cottage industry designed and run by doctors, health administrators and third parties.
3. It needs reform and reorganization so that it is consumer oriented and, apparently, consumer run.
4. Good medical care is a right to which there is universal entitlement. To provide good care is a privilege, and it should be convenient.
5. Doctors are too research oriented and too trained in the sciences and too ignorant of the social implications and the interpersonal needs of their patients. Ivory tower educators are at least *an* important source of this problem.
6. The system should be financed by the Federal Government and run locally with minor variations (local, city, county, state).
7. The problems, blame and solutions should be shared. There is no magic here. The problems must be isolated; programs devised and started.
8. Too many politicians have fifty-second solutions and expect magical responses to their speeches.

9. Inspector generals of the medical system would solicit and collage criticisms. They would correct inequities, weigh changes and probably discipline.

10. We should broaden the base of health care professional applicants—doctors, dentists, nurses, paramedics—to include more minority students to help get these professionals back to the inner city, the Indian reservations, etc. (Do they often return to the slums and to the home country after training here? We must cast at least a glance at a social system which negates hard work but demands instant status and gratification.)

11. We should require two years of obligatory service for all doctors in government designated areas of high medical need.

Summary: Overall I liked the book but didn't like being included by inference as one who neglects the niceties of interpersonal relations, favors maldistribution of medical care, rakes in the money, resists change required for the overall good, and educates students subtly and by precept to ignore the personal and medical needs and dignity of patients.

Rate "B+" in liberal milieu and "C" in conservative climate.

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Information to Authors of Manuscripts Submitted to The Medical Annals of the District of Columbia

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The entire manuscript, including footnotes and case reports, should be submitted unrolled, with double type spacing. An original copy and one carbon copy should be submitted, and a carbon copy should be retained by the author.

The title should not exceed 80 characters and spaces. If a subtitle is used, it should not be connected grammatically to the main title.

The by-line, the author's given name and initial or given name alone should be supplied. The M.D. degree or highest academic degree should be listed for each author. Not more than six names should be included as authors, unless the communication is the report of a committee.

The footnotes, hospital and university affiliation when study was done, should be listed. Present affiliation and location (if different from that at time of study) should be given. Acknowledgements should be limited to persons, foundations, agencies or companies supplying drugs, funds or apparatus free of charge or otherwise making an extensive contribution to the study.

REFERENCES

The number of references should not exceed 18 single complete bibliographic citations, except in Special Articles.

References should be double spaced, on a separate sheet, and listed in order of citation in the text. Superior numbers should be inserted in the text at points of citation.

References should be given in the style regularly used in THE ANNALS, eg:

Seremetis, M.D., DeGuzman, V.C.,
Lyons, W.S., Peabody, J.W.: Complications of Cardiac Pacemakers, Medical Annals of D.C., 1973, 42, 165.

TEXT

Use generic or descriptive names of drugs when available. Trade names, capitalized, may be given in parentheses when the drug is first mentioned.

Statistics should be checked for consistency within the text and for agreement with graphs or tables.

Laboratory data should not be given in abbreviated form but in full (e.g., "hemoglobin level, 12 Gm. per 100 ml." rather than "Hb. 12 GM.%).

Figures should be used for number 10 and above, laboratory measurements, percentages, and ages.

Metric equivalents should be given for dosage and body height and weight.

Centigrade equivalents should be given for Fahrenheit body temperatures, and vice versa.

Abbreviations should be used sparingly, with expansion given for those not listed in standard medical dictionaries.

The meaning of "we" should be clarified, especially if there is only one author. Avoid use of editorial "we."

SUBHEADINGS

One center heading should be supplied for about every three pages of double-spaced text copy. Subdivisions of main topics should be indicated by side headings.

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The summary should be brief, giving specific facts concerning the study and its results.

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The street address of one author should be given at the end of the article for reprint requests and correspondence.

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The title should be given at top of the page for each table.

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The meaning of abbreviations should be clear, with those not listed in standard medical dictionaries expanded in a footnote to the table.

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Arrows should be inserted to pinpoint lesion or any important feature.

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INDEX TO ADVERTISERS

Equipment and Supplies

Kloman Surgical Supply Company 40

Insurance

Corroon & Black, Russel, Inc. 40

Mutual of Omaha 2

Ralph W. Lee & Company 55

Nurse Registries

Association of Undergraduate and

Practical Nurse Registry 53

District of Columbia Manpower

Administration 40

Nutrition Education

Dairy Council of Greater Metropolitan

Washington, D.C. 4

Pharmaceuticals

Burroughs Wellcome & Company 37

Burton Parsons & Company 37

Flint Laboratories 34-35

Eli Lilly & Company 6

McNeil Laboratories 2

Pharmaceutical Manufacturers

Association 7

William P. Poythress & Company 3

Reed & Carnick 3

Roche Laboratories 2-3, 42, C3, C

G. D. Searle & Company 30-3

The Upjohn Company 46-4

Pharmacy

Peoples Drug Stores 4

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Checks, etc. should be made payable to the Medical Society of the District of Columbia.

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Indications: Relief of anxiety and tension occurring alone or accompanying other disease states.

Contraindications: Patients with known hypersensitivity to the drug.

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Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg, or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and irritability) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, espe-



cially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests

advisable during protracted therapy.

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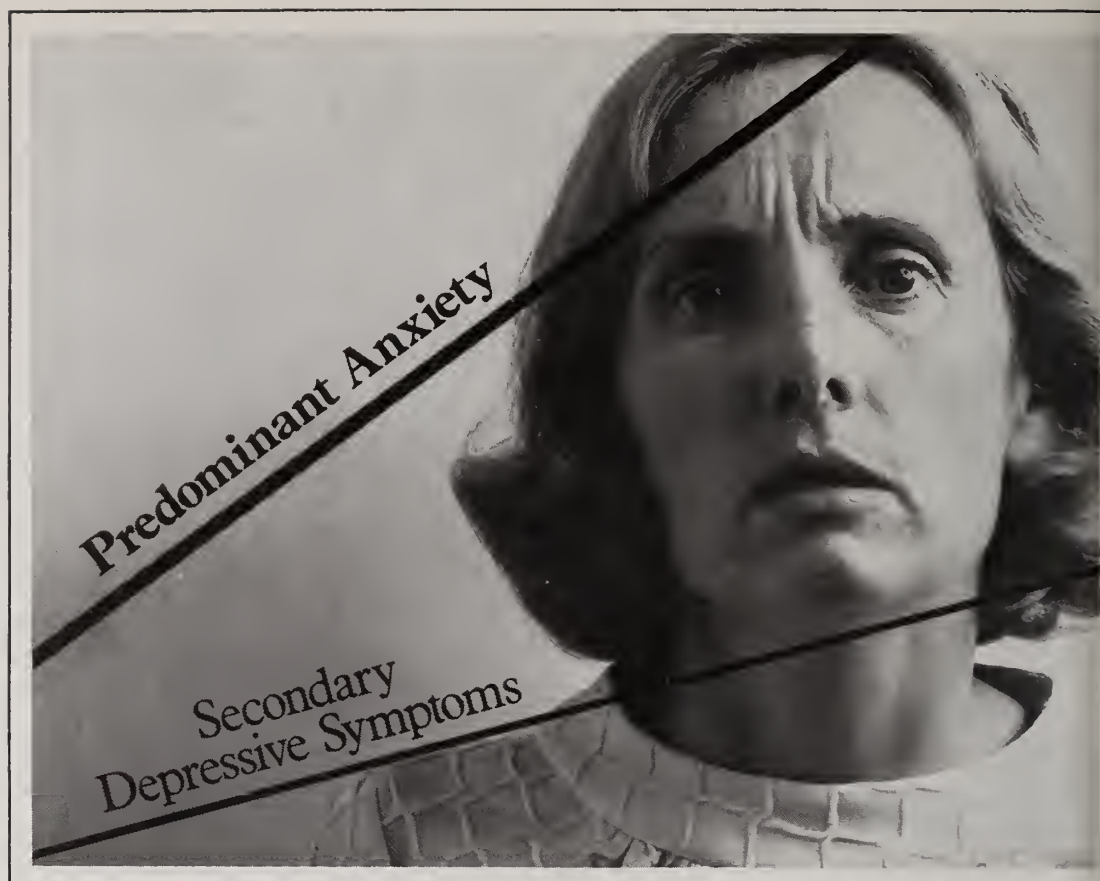
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CONTENTS

SCIENTIFIC ARTICLES

Psychological Aspects of Intensive Care Units. Harry S. Abram, M.D.	59
Continuous Infusion of Diazepam in Infants with Severe Recur- rent Convulsions. Y. H. Thong, M.B., B.S. and David C. Abram- son, M.D.	63
Actinomycosis Arthritis: A Case Report. Peter B. Sherer, M.D. and John Dobbins, M.D.	66
The Use of Immunosuppressive Agents in Takayasu's Arteritis. Hubert J. Alpert, M.D.	69
Sympathetic Beta Adrenergic Blockade in the Preoperative Treatment of Hyperthyroidism. Arnold G. Brody, M.D. and Robert Dibble, M.D.	72

OTHER FEATURES

President's Message	5
Communication. Clifton R. Gruver, M.D.	
Editorial	6
The Dangerous Sex Offender. David A. Lanham, M.D., F.A.P.A.	
Post Graduate Education	93
Adult Respiratory Distress Syndrome. Hall G. Canter, M.D.	
Book Reviews	99
Gastroesophageal Reflux in Hiatal Hernia. (Skinner, Belsey, Hendrix and Zuidema) Reviewed by Stuart H. Danovitch, M.D.	
Aging and Mental Health. (Butler and Lewis) Reviewed by John Stubenbord, M.D.	
Labor-Management Relations in the Health Services Industry. (Metzger and Pointer) Reviewed by Harold L. Hirsh, M.D.	
Medical Education in the United States Before the Civil War. (Norwood) Reviewed by Bruce I. Shnider, M.D.	
Information for Authors	104
Advertising and Subscription Information	106
Index to Advertisers	106

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PRESIDENT'S MESSAGE

COMMUNICATION

One of my friends asked at a gathering the other night, what was to be my "Theme" for 1974?

I replied: The scope of involvement of the Medical Society is so vast as to provide a number of possible themes. But one of those heading my list would be communication.

My friend said: He has belonged to this Society for 30 years and no one has ever sought his opinion—said his opinion had never been "polled". That provocative phrase struck a responsive chord. An idea began to jell—not a new one, but perhaps one our Society could utilize to greater potential—an opinion survey.

We have a large Society—some 2,000 active members—and this includes physicians from all walks of the profession: private practitioners, those in primary care, specialists, solo practitioners, groups, clinics; fee-for-service practice, prepaid plans-HMO's; researchers, teachers, students, house officers; employees of industry and of government, inner city, suburbia, minority groups, and so on.

Our diversified profession also needs appropriate dialogue to learn another's views, and to understand the problem areas, needs, and responsibilities that may lie beyond our own immediate sector. Which means, knowing how we think and knowing where there is agreement and disagreement, and why.

The keystone for this understanding and dialogue is adequate communication. We must listen to one another and thus develop our opinions constructively through an educational exchange of ideas.

One of the weaknesses of a poll, however, lies in its potential for inadequate (or non-representative) response. Our Society's response in past surveys has been good. Certainly, general trends of member opinion has been evident, and has been born out by the status of such national pollsters as Gallup and Harris. The AMA has also had success with this method.

Within the Society's Constitution and Bylaws, there is, of course, the power of the vote itself, by each individual, on major policy issues. In an earlier editorial, I indicated the usefulness of committee service for expression of opinion, and, in addition, any member is welcome to call or write the Society regarding his views.

But there is room for other vehicles of communication.

An opinion poll might prove a useful adjunct to the other measures of communication, members to leadership, and vice versa.

I would like to see us close our ranks and put our shoulders to the wheel together to achieve the common goal of ever-improving medical knowledge and skill for the benefit of both the health and well-being of the individual and the community.



CLIFTON R. GRUVER, M.D.
PRESIDENT

A handwritten signature in dark ink that reads "Clif Gruver". The signature is written in a cursive, flowing style.

Editorial

The Dangerous Sex Offender

I am motivated to write this article by the recent public shock surrounding several sadistic sexual attacks and related murders in this metropolitan area. I believe that there is a great deal of ignorance of the facts concerning potentially dangerous sex offenders in the area. It may well be that many people do not really want to know how complex the issue is. However, it seems appropriate that those of us who deal with these individuals on a continuing basis should share information, and responsibility, with others in the community.

It is extremely difficult to get an accurate census of how many and what types of sex offenders are in the Washington, D.C. Area, which of course encompasses adjoining areas of Maryland and Virginia. As one index of the extent of the problem, the annual report of the Washington, D.C. Police Dept. for Fiscal Year 1972 lists 670 rape offenses and 318 sex offenses exclusive of prostitution. These figures do not include the suburbs, and it is generally accepted that many rapes and other sex offenses go unreported because of the legal hassles, embarrassment, and shame involved for the victim. If we include under the heading of sex offenders exhibitionists, voyeurs, pedophiles (both homosexual and heterosexual child molesters), sexual sadists, and rapists, we are talking about a very large population indeed. I have not even included incest cases occurring within families with both natural and step-children. Exhibitionists and voyeurs must be included in the group because while they usually do not pose a physical threat to their victims, it is not really possible to say that they are not dangerous until they are properly evaluated. For example, a few exhibitionists do attack, and some voyeurs are only "casing the joint" before breaking and entering.

Hundreds of such offenders are processed through the judicial systems of the District of Columbia and adjoining jurisdictions each year. The public should not be under any illusion that such offenders are found only in the District of Columbia. This means that the number of known sex offenders both from the recent past and in the present who are known in the Courts, probation offices, parole offices, psychiatric hospitals (both public and private), as well as private physicians, psychiatrists and psychologists number in the thousands. To this number we must add the numbers in correctional institutions serving sentences, awaiting trial, out on bail and bond, etc.

It seems to me that in many ways this population actually could well be thought of as a Public Health problem of considerable magnitude. It is an understandable exercise in futility for the media and the public to cry out in pain and alarm each time there is a horrible, vicious case and to attempt to fix blame for the individual case. This is a very large problem, it will not go away, it could be ameliorated but the community must be willing to pay the price.

There are many frustrating paradoxes involved in the problem of the management of sex offenders. For example, many call for all potentially dangerous sex offenders to be "locked up", and/or summarily executed or castrated. However, at the same time, commissions and groups are advocating virtual abolition of penal institutions and mental hospitals, and the whole thrust is toward rehabilitating offenders in the community. Also, civil liberties groups, often quite properly, are bent on the protection of the rights of the accused and the committed. It is also a fact that many of those in the community who want dangerous offenders locked up or better controlled, are by no means ready to pay increased taxes for decent institutions in which to maintain and attempt to rehabilitate them or for more probation officers, parole officers, and behavioral scientists to work with such offenders.

In my opinion there are also racial and social attitudes involved in some of the reactions to violent sex crimes. The outcry and publicity is great when such offenses occur in places and against persons where they are not expected or somehow not supposed to occur. However, inner city black people are victimized by sex offenders with considerable frequency and I have been impressed by how remarkably little notice has been taken of some of these events which have come to my attention. The tragedy is every bit as real and great, no matter who the victim.

We are dealing with an extremely large and difficult group of individuals with a very fallible and often inadequate human system. Every day Judges and others working within that system must give opinions and make very difficult decisions, in attempting to manage these offenders with what the community is willing to allot for that purpose. All potentially dangerous sex offenders can never be "locked up". The safety of the community must be continually balanced against the civil rights of

individuals. For instance, many attorneys have raised serious questions about the constitutionality of indeterminate sentences for so-called sexual psychopaths or "defective delinquents", and the right to bail or bond must always be respected.

Even if many dangerous sex offenders are incarcerated it would not eliminate the first offender, the offender who has not yet been apprehended or identified, or who comes in from other areas. Similarly, every day dangerous sex offenders walk out of prison by expiration of sentence. Very little seems to be made of this, perhaps because it is believed that they have "paid their debt to society", when in actuality there has been little or no real effort at rehabilitation and/or treatment of the underlying psychological disturbance. In that vein, it also should be clearly stated that many sex offenders are very disturbed individuals, ranging all the way from clearly psychotic persons through the whole diagnostic manual of mental diseases (including organic conditions). This is by no means a problem which can be approached from a moralistic point of view.

Our society does not seem to like to face problems

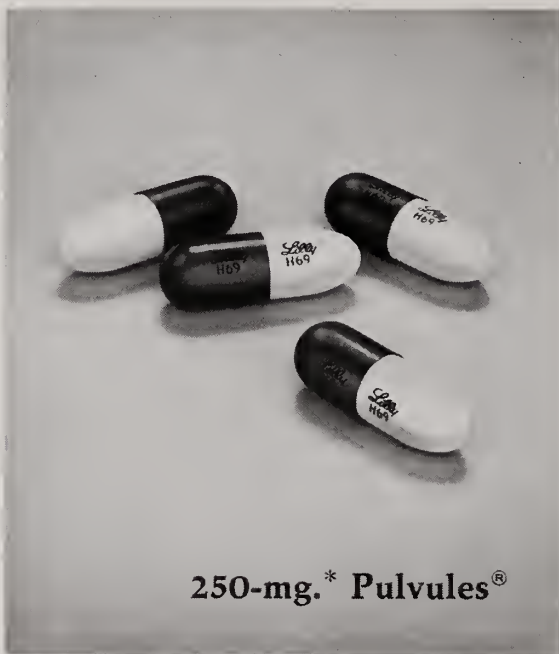
for which there are no straight-forward or simple solutions. The problems involved in aberrations of sex and aggression in human beings are more complex than the technical and engineering problems of getting to the Moon. I believe that it is extremely important that physicians and other responsible persons as well as the general public have a better understanding of the scope of this problem and some of the issues involved. There have been sex offenders in all societies. We can work to minimize the problem by early identification, more knowledge and better management. We need more money; however, no matter how much money is spent there will be failures of rehabilitation and treatment and there will continue to be violent sex offenses committed in our community. To a considerable degree I believe the responsibility must be shared by all of us for improving that community and making a more human environment. This is the only hope for true progress with this very difficult problem.

DAVID A. LANHAM, M.D., F.A.P.A.

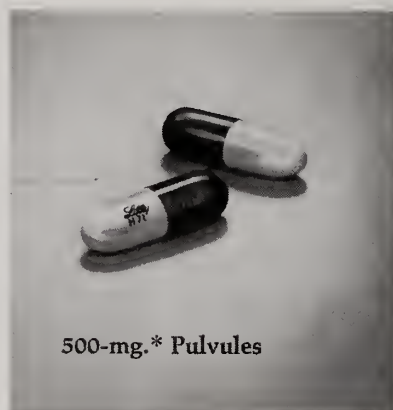
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SCIENTIFIC ARTICLES

Psychological Aspects of Intensive Care Units*

HARRY S. ABRAM, M.D.

The psychology of intensive care units represents a complex issue, not only because its newness but for the wide variety of situations included under the term "intensive care." It is likely that the "intensive care syndrome" is a misnomer. McKegney¹ used the term to describe "psychological and behavioral disturbances which are arising more frequently as increased numbers of cardiovascular recovery rooms, coronary care units, chronic dialysis facilities, and other intensive treatment programs are developed." He concluded, "The 'intensive care syndrome' is a new disease of medical progress, manifesting itself in a variety of newly developed treatment situations."

In years to follow no new disease or specific syndrome emerged. Contrariwise some psychiatric studies have refuted McKegney's² remarks, and yet one continues to hear of this ill-defined syndrome and that psychiatrists believe that ICU environmental stresses are the sole etiological agents involved in post-cardiotomy psychoses. In order to clarify these misconceptions, one must look at several facets of the problem: the psychological disturbances which occur; the differences in intensive care, coronary care, and renal dialysis units; and the reactions of the nursing personnel to the psychological stresses inherent in these varied environments.

Open-heart Procedures and the ICU

The major psychiatric complication following open-heart operations is that

of delirium, first described by Blachly³ as "post-cardiotomy delirium." In his series of 139 patients it occurred in 57% and was characterized by disorientation, memory loss, impaired judgment and other clinical signs of transient brain insult. Blachly minimized the importance of psychological and premorbid personality factors in the development of this psychotic state. In the same year Egerton and Kay⁴ reported their findings in 90 adults undergoing open-heart procedures, 40% of whom were delirious in the post-operative phase. These investigators emphasized sleep deprivation and "abnormal sensory input" and concluded that "The recovery room situation, which was regarded as an ordeal by most adult patients, would appear to be largely responsible for the production of delirium." Egerton noted that the delirium "was often preceded by one or two sleepless nights..." (and) "Apart from brief visiting periods and times of staff care, for a few days the patient's visual field was restricted to white acoustic tiling viewed through an oxygen tent. Many patients remarked on the monotony of the ceiling, and visual hallucinations were often initially manifested by the appearance of patterns on the ceiling or of faces protruding from the small, regular holes in the tiling." He mentioned other predisposing and precipitating factors, such as previous brain damage, dehydration and hyponatremia.

Kornfeld and his co-workers⁵ found that 38% of a series of adult open-heart patients "experienced some of

the manifestations of a psychotic-like syndrome in the recovery room." Kornfeld observed, "The patient might first experience a perceptual distortion—for example, the sound arising from the air-conditioning vent might begin to sound like his name. In some patients these distortions of reality progressed to the point of auditory or visual hallucinations and then to frank paranoid delusions." There was also "transient disorientation," and "in most cases the psychotic symptomatology began its slow evolution after a lucid interval of about three to five days." Generally the psychosis "cleared within 24-48 hours after transfer to the standard hospital environment."

Abram⁶ described a psychotic phase after open-heart surgery closely resembling reality distortions associated with sensory deprivation experiences, and commented upon the estranged environment in the ICU. He wrote, "The patients often associated the ICU with severe discomfort, waking up after surgery, tracheotomies, intravenous fluids, the cardiac pacemaker, and the monitoring devices. Several believed that they improved only after leaving the ICU and looked upon going back there as a death warrant. The apparatus in this unit, the hushed tone of the doctors and nurses hustling about in an urgent fashion caring for critically ill patients, the starkness and sterility of the room and the placement of tubes in every conceivable orifice leave ample grounds upon which to base paranoid delusions."

There are many complexities of

PSYCHOLOGICAL ASPECTS OF INTENSIVE CARE UNITS

ABRAM

psychoses following open-heart operations outside the purview of this presentation which are covered elsewhere.⁷ Suffice it to note that they frequently occur (postoperatively in the realm of 40% to 60% as compared to less than 1% after general surgical procedures), are usually transient, and that ICU milieu has been implicated as one but by no means the only etiological agent in their development. Central nervous system dysfunction, severity of illness, length of time on the pump-oxygenator, the adequacy of preoperative psychological preparation, postoperative anxiety, cerebral hypoxia, and the possibility of circulating amines are merely a few of the other variables postulated as causative. Undoubtedly post-cardiotomy delirium is multidetermined and can take a variety of forms, ranging from mutism and withdrawal to panic, confusional states and hallucinatory-delusional disorders.

It is not surprising that some of the most vivid accounts of these psychoses are autobiographic. As an example, Kesten⁸ wrote of his postoperative experiences:

"Either I was having a nightmare, or I was dead and in hell. I elected for the latter. Of course, I must be in hell. I couldn't be dreaming such things. The snakes, the jumping grasshopper, the tubes stuck in my body, the neon lights, . . . the maddening whirling sound, the coughing, the gash in my chest—Hell! Let me out of here! It's all a mistake!"

MacKenzie⁹ wrote of similar episodes.

Coronary Care Units

When one turns to other forms of intensive care the occurrence of acute disruptive behavior is by no means consistent with that described in the post-cardiotomy patient. In studies of psychological responses of patients to coronary care units most investigators

report that the CCU atmosphere and monitoring are reassuring rather than menacing. Delirium is rarely mentioned. Only one report devotes itself solely to the subject. In it Parker and Hodge¹⁰ related "sensory monotony and sleep deprivation" to the onset of delirium in myocardial infarction patients in coronary care units, and yet it occurred in only 11 of 500 patients treated in their units.

Hackett and his co-workers^{11,12} found the psychological hazards in the CCU minimal and concluded that "man is the doughty survivor rather than a victim of the modern technology that, while saving his skin, can wreck his life." Cardiac monitoring, in contrast to findings in the ICU in which post-cardiotomy patients ironically project their fears and hostilities upon life-saving devices, was regarded as protective, or as one coronary patient remarked as a "mechanical guardian angel." In place of panic and psychosis and with the use of denial as a major defense mechanism CCU patients "seem able to extract the positive meanings from the most bleak circumstance and to enlarge upon them while ignoring or minimizing the truly lethal implications of their condition." Dominian and Dobson¹³ corroborated Hackett's conclusions. In their study only six out of 74 men found the CCU anxiety-producing, and in general their "overall results suggest that a coronary care unit has minimum adverse psychological effects on patients." As one patient stated, "machinery means efficiency. If something does go wrong there must be more chance of putting you right with all this equipment." Klein's¹⁴ findings of increased anxiety and elevated levels of urinary catecholamines in patients at the time of transfer from coronary care units substantiated that feelings of dependency and comfort appear to be associated with the patient's stay on such units and that transfer can disrupt this sense of security.

There is less agreement on the psychological effects of survivors of cardiac arrest. In Druss and Kornfeld's study¹⁵ of ten such survivors the psychological aftermath was severe. Following their resuscitation in a cardiac monitoring unit many were plagued with "frightening and violent dreams." After discharge from the unit both the survivors and a comparative group of myocardial infarction patients without cardiac arrest exhibited "long-standing emotional problems including insomnia, irritability, and a restriction of their activities often beyond what was medically appropriate." The results of Dobson¹⁶ and Hackett¹² are less "gloomy." Both found less evidence of traumatic neuroses and did not report major problems with rehabilitation in cardiac arrest patients after discharge from the hospital. Again a biographical account, in this instance of a physician who experienced a cardiac arrest,¹⁷ gives valuable insight into the emotional aspects of this situation. In a discussion of the episode the resuscitation registrar involved in the physician's care stressed the "value he (the physician) attached to contact with other human beings during the twenty hours after his arrest."

Chronic Dialysis Units

The psychiatric complications of chronic dialysis for terminal renal failure are only indirectly related to the unit in which it is performed. Indeed for economic as well as for psychological and other reasons there is a trend toward home programs rather than hospital-centered dialysis. When dialysis was initially used clinically and carried out in a research (as opposed to treatment) setting, there were episodes¹⁸ of "schizophrenic-like" psychoses while patients were being dialyzed. Cooper¹⁹ reported a woman dialyzed with a hypomanic psychosis. Her delusions centered

around the dialyzer ("the monster") upon which she projected considerable hostility and rage. Other dialysands have reported fantasies of personifying the dialyzer, looking upon it as an extension of themselves, or incorporating it into their body schema whereby they become machine-like. These fantasies resemble some aspects of the delusional material related to the monitoring devices observed in post-cardiotomy deliria. However, as dialysis became an accepted mode of treatment and units were established devoted entirely to caring for the chronic dialysand, reports of acute psychiatric disturbances were rare. In essence one moved from the crisis situation of the intensive and coronary care unit to the more subtle and long-term problems and conflicts of the chronically ill patient. Such perplexing issues as the prolongation of life in the patient who seemingly could not tolerate or elected not to tolerate the rigors and constrictions of dialysis came to the fore. Depression, inability or unwillingness to maintain dietary restrictions, and self-destructive behavior became evident.²⁰ Although these reactions occur outside the dialysis unit, they nevertheless represent important by-products of intensive care and advancing medical technology.

Psychological Stresses of the Intensive Care Nurse

In all of the intensive care situations under discussion interpersonal and intrapersonal conflicts as they affect the nursing personnel in their relationship with patients and physicians require mention and consideration. In intensive care unit nursing Vreeland and Ellis²¹ and later Hay and Oken²² noted sources of anxiety in this form of work related to feelings of insecurity in knowledge or skill, the burden of responsibility in caring for the critically ill, repetitive exposure to death and dying, object loss with the

death of patients, work overload, lack of gratification, and intragroup tensions. The "turnover" rate of ICU nurses with their moving on to less stressful situations and the frequency with which they develop psychosomatic disorders can be high. It is of interest and probably indicative of a less stressful environment that CCU nurses rated "heavy lifting" most frequently as a source of frustration.²³

With chronic dialysis nurses one encounters countertransference problems of overidentification and involvement with the patients. It is not unusual for nurses to report dreams in which they themselves are being dialyzed or have arteriovenous shunts similar to their patients.²⁴ Often such unresolved difficulties can impede the patient's independence so essential for successful rehabilitation or lead to discouragement or disillusionment in the personnel when a death on the unit occurs.

Discussion

"... if they would give me back my watch, must now be morning. There are no windows though to judge that by, only those cones of light trained on our eyelids... high iron grills fencing in each of the nearly touching beds constantly being (one man dying or making gurgling sounds of death, another in new-bloodied bandages arriving) trundled in or out."

These lines²⁵ are but a few telling of a poet's ordeal in an intensive care unit. It seems apparent that he is expressing the thoughts and feelings of other patients going through similar experiences. Yet it is also apparent that intensive care units, coronary care units, and renal dialysis units cannot be categorically called "stressful" and that one must carefully evaluate the meaning of each to the patient in the

context of his disease and its treatment. Dealing with the acute threat of open-heart surgery and its physiological effects in an ICU environment is obviously different from undergoing treatment for a myocardial infarction in the atmosphere of a CCU or living with the long-term tensions of chronic renal disease and dialysis. In a similar fashion it would be simplistic to look upon post-cardiotomy delirium as "caused" by the ICU environment when its etiology appears so multifactorial in nature.

Yet there are some common threads in all of these situations which allow for some overall therapeutic principles to aid the patient.

1. Adequate patient preparation. In general the more informed a patient is the better he is able to cope with the psychological stress. There is evidence that establishing a preoperative relationship with a patient undergoing an open-heart procedure,^{26,27} including explanations of the post-operative phases and ICU practices, decreases significantly the occurrence of post-cardiotomy delirium. Likewise, preparing the patient in as much advance as possible for transfer from a CCU decreases anxiety at the time of moving back to the regular hospital ward. Preparation should also include the family. Warnings of the possibility of post-cardiotomy delirium may alert family members and allay fears that the patient has become incurably insane if psychosis appears.

2. Ongoing human contact. Adequate preparation is not enough in itself. A familiar face and continued interest can decrease the panic of a critically ill patient. The physician-patient relationship remains a powerful therapeutic measure. Such contact should not be ignored in the semi-comatose patient for whom reassuring words (and conversely careless statements) have great meaning.

3. Increasing sensory input. There is also evidence that allowing adequate

PSYCHOLOGICAL ASPECTS OF INTENSIVE CARE UNITS

ABRAM

sensory cues decreases post-operative psychoses. Wilson,²⁸ for example, demonstrated that delirium was three times greater in a windowless recovery room than in one with windows. Kornfeld⁵ made other suggestions along this line, such as having clocks and calendars in ICUs.

4. Allowing consideration of the nurse's role and frustrations. Group sessions have proved helpful in some ICU settings for the resolution of intragroup tension.²² Certainly the observation²⁹ that, "In the final analysis, the success of a coronary care unit depends not on the sophistication of the electronic equipment within it but on the ability, dedication, and *esprit de corps* of the personnel who work in the unit" speaks to the importance of the nurse's role and morale.

Through an ongoing relationship and with these maneuvers we may be of some help to the patient in his struggle with life and death—a struggle intimately involved in the surroundings of intensive care during which each patient asks the "crucial question" raised by Solzhenitsyn:³⁰

"Each bed was a closed world, where a unique struggle was being waged in a unique body, each man asking himself the crucial question: will I live or not?"

References

1. McKEGNEY, F. P.: The intensive care syndrome. *Conn Med* 30:633-636, 1966.
2. SGROI, S., HOLLAND, J., MARWIT, S. J.: Psychological reactions to catastrophic illness. *Psychosom Med* 30: 551-552, 1968.
3. BLACHLY, P., STARR, A.: Post-cardiotomy delirium. *Amer J Psychiat* 121:371-375, 1964.
4. EGERTON, N., KAY, J. H.: Psychological problems associated with open-heart surgery. *Brit J Psychiat* 110:433-439, 1964.
5. KORNFELD, D. S., ZIMBERG, S., MALM, J. R.: Psychiatric complications of open-heart surgery. *New Eng J Med* 273:286-292, 1965.
6. ABRAM, H. S.: Adaptation to open-heart surgery: a psychiatric study of responses to the threat of death. *Amer J Psychiat* 122:659-668, 1965.
7. ABRAM, H. S.: Psychotic reactions after open-heart surgery, a critical review. *Sem in Psychiat* 3:70-78, 1971.
8. KESTEN, Y.: *Diary of a Heart Patient*. New York, McGraw-Hill, 1968.
9. MacKENZIE, R.: *Risk*. New York, Viking Press, 1971.
10. PARKER, D. L., HODGE, J. R.: Delirium in a coronary care unit. *JAMA* 201:702-703, 1967.
11. HACKETT, T. P., CASSEM, N. H., WISHNIE, H. A.: The coronary care unit: an appraisal of its psychological hazards. *New Eng J Med* 279:1365-1370, 1968.
12. HACKETT, T. P.: The Lazarus complex revisited. *Ann Int Med* 76:135-136, 1972.
13. DOMINIAN, J., DOBSON, M.: Study of patients' psychological attitudes to a coronary care unit. *Brit Med J* 4:795-798, 1969.
14. KLEIN, R. F., KLINER, V. A., ZIPES, D. P., et al: Transfer from a coronary care unit: some adverse responses. *Arch Int Med* 122:104-108, 1968.
15. DRUSS, R. G., KORNFELD, D. S.: The survivors of cardiac arrest: a psychiatric study. *JAMA* 201:75-80, 1967.
16. DOBSON, M., TATTERSFIELD, A. E., ADLER, M. W., et al: Attitudes in long-term adjustment of patients surviving cardiac arrest. *Brit Med J* 3:207-212, 1971.
17. Both Ends of the Stethoscope, Cardiac arrest. *Lancet* 1:262-264, 1969.
18. SHEA, E. J., BOGDAN, D. F., FREEMAN, R. G., SCHREINER, G. F.: Hemodialysis for chronic renal failure: IV. Psychological considerations. *Ann Int Med* 62:558-563, 1965.
19. COOPER, A. J.: Hypomanic psychosis precipitated by hemodialysis. *Comp Psychiat* 8:168-174, 1967.
20. ABRAM, H. S.: Suicidal behavior in chronic dialysis patients. *Amer J Psychiat* 127:1199-1204, 1971.
21. VREELAND, R., ELLIS, G. L.: Stresses on the nurse in an intensive care unit. *JAMA* 208:332-334, 1969.
22. HAY, D., OKEN, D.: The psychological stresses of intensive care nursing. *Psychosom Med* 34:109-118, 1972.
23. CASSEM, N. H., HACKETT, T. P.: Sources of tension for the CCU nurse. *Amer J Nurs* 72:1426-1430, 1972.
24. FOY, A. L.: Hemodialysis: dreams of patients and staff. *Amer J Nurs* 70:80-82, 1970.
25. GUTHRIE, R.: *Maximum Security Ward*. New York, Farrar, Straus & Giroux, 1970.
26. LAZARUS, H. R., HAGENS, J. H.: Prevention of psychosis following open-heart surgery. *Amer J Psychiat* 124:1190-1195, 1968.
27. LAYNE, O. L., YUDOFISKY, S. C.: Postoperative psychosis in cardiotomy patients. *New Eng J Med* 284: 518-520, 1971.
28. WILSON, L. M.: Intensive care delirium. *Arch Int Med* 130:225-226, 1972.
29. Report: Training Techniques for the Second Bethesda Conference of American College of Cardiology, 1965.
30. SOLZHENITSYN, A.: *August 1914*. New York, Farrar, Straus & Giroux, 1971.

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Continuous Infusion of Diazepam in Infants with Severe Recurrent Convulsions

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Abstract:

Five infants with severe recurrent convulsions secondary to acute cerebral insults and refractory to conventional anticonvulsive therapy were treated with continuous intravenous infusion of diazepam. The results indicate that this mode of therapy is both safe and effective in controlling refractory seizures, and successfully prevents their recurrence.

Introduction

The mechanism or mechanisms by which severe convulsions produce cerebral injury or death is unclear. Anoxia resulting from respiratory difficulties during the seizure may play a role. However, in a study on cats, induction of prolonged seizures resulted in the death of all animals within eight to forty-eight hours even though adequate oxygenation was maintained.¹ These findings suggest that in the management of status epilepticus, control of cerebral dysrhythmia is as important as providing cardiorespiratory support.

Parenteral diazepam has received endorsement as a safe and effective drug for acute seizure control in children.²⁻⁶ However, its usefulness is limited by its relatively short duration of action. In this report, we describe the use of diazepam by continuous intravenous infusion in five pediatric patients with severe recurrent convul-

TABLE 1: SUMMARY DATA OF FIVE PATIENTS WITH SEVERE RECURRENT CONVULSIONS TREATED BY CONTINUOUS DIAZEPAM INFUSION

Patients	Diagnosis	Dosage* & Duration
1. D.T., male 6 wk, 4.4 Kg	Acute gastroenteritis Hypernatremic dehydration Congestive cardiac failure	3 mg/Kg/day × 6 days
2. C.L.D., female 7 wk, 5.2 Kg	Cardiorespiratory arrest Ventricular extrasystole	4 mg/Kg/day × 5 days
3. B.C., female newborn, 3.0 Kg	Birth asphyxia	8 mg/Kg/day × 6 days
4. C.J., male 3½ mth, 5.0 Kg	Laryngotracheomalacia Combined immunodeficiency Truncus arteriosus	5 mg/Kg/day × 18 days
5. M.T., male 13 mth, 11.4 Kg	Bronchitis Pneumonia Encephalitis	12 mg/Kg/day × 21 hours

* Denotes maximal dosage attained during the period of treatment.

sions secondary to acute cerebral insults and refractory to conventional anticonvulsive therapy. Although this mode of administration has been employed for seizure control in three patients,⁶⁻⁸ neither the safety nor efficacy of the procedure, nor the effective dosage levels have been determined.

Case-reports

A summary of patient data is presented in Table 1. The clinical course of each patient is discussed below.

Case 1: This six week old infant was transferred from another hospital with

congestive cardiac failure and severe recurrent convulsions following correction of hypernatremic dehydration secondary to acute gastroenteritis. The seizures were resistant to several doses of phenobarbital, paraldehyde, and diazepam with frequent recurrences. After the initiation of continuous diazepam therapy, the convulsions became well-controlled, with only four breakthrough seizures during the first twenty-four hour period, each being brief and spontaneously resolving, and no longer accompanied by apneic spells. Spasticity and ankle clonus gradually diminished. He remained drowsy for the duration of therapy, but was easily arousable and able to

INTRAVENOUS DIAZEPAM IN INFANTS WITH CONVULSIONS

THONG AND ABRAMSON

bottle-feed the next day. On discharge after 10 days of hospital stay, he had a normal EEG and physical examination.

Case 2: This seven week old infant went into sudden respiratory arrest at home two days after developing upper respiratory infection symptoms. Cardiac arrest in the Emergency Room was reversed by means of intracardiac epinephrine and electrocardioversion. Subsequent development of recurrent seizures with apneic attacks required the continuation of artificial ventilation. Within an hour of starting infusion diazepam, apneic attacks were abolished, and the child was weaned off the respirator. One brief breakthrough convulsion occurred over the first twenty-four hour period. Lidocaine was administered for treatment of ventricular arrhythmia which was presumably a complication of cardioversion. She was discharged one week later in good physical condition. Follow up at three months revealed no cardiac or neurological deficits.

Case 3: This newborn was asphyxiated at birth. Two hours following successful resuscitation severe convulsions and apnea developed. Treatment with phenobarbital, dilantin, paraldehyde, and diazepam did not prevent frequent recurrences. Initial therapy with 4 mg/Kg/day abolished the apneic attacks, but increased doses of 8 mg/Kg/day were needed for adequate seizure control. She was discharged after ten days in the intensive care nursery without detectable neurological deficit.

Case 4: This three-and-a-half month old boy had multiple congenital abnormalities which included laryngotracheomalacia, immunodeficiency, and truncus arteriosus. Transient laryngeal occlusion and anoxia resulted in a convulsive disorder amenable to phenobarbital at 6 mg/kg/day. Following a second episode of laryngeal occlusion two weeks later, infusion diazepam was instituted for the control of

recurrent convulsions. He expired after two months of hospital stay from cardiac complications.

Case 5: This thirteen month old was admitted with a viral syndrome comprising encephalitis, bronchitis and pneumonitis. Initial seizures were controlled with phenobarbital, dilantin and intermittent injections of diazepam. On the fourth day of admission, he went into status epilepticus. He required 12 mg/Kg/day of diazepam by constant infusion for control. There was residual neurological damage as a consequence of the severe encephalitis.

Discussion

Diazepam is not soluble in water. On dilution in parenteral fluids, it forms a fine cloudy suspension. Others^{2,9} as well as ourselves have not found this to adversely affect its pharmacological properties. When administering diazepam by continuous intravenous infusion, a suitable dose of the drug is diluted in a volume of parenteral fluids required by the patient in each six to eight hour period. Agitation of the solution by hand every half-hour ensured even distribution of the medication.

The effective levels of diazepam for the control of severe recurrent convulsions in our series ranged from 3 to 12 mg/Kg/day. Toxic manifestations attributable to diazepam were not observed. Patients on these doses were drowsy but easily aroused. In animal experiments, the drug was shown to possess a wide margin of safety.¹⁰ The highest tolerated dose in man is not known. To date the highest dosages reported in clinical usage were 720 mg/day in a 57 Kg man,¹¹ and 120 mg/day in a 3 Kg neonate.¹² At dosages of up to 12 mg/Kg/day and higher in the treatment of tetanus neonatorum, significant toxic effects were not encountered.¹³⁻¹⁵

Respiratory arrest is a potential

hazard of diazepam therapy. A total of eight cases have been reported in the pediatric age group.^{2,5,6,8,16,17} This complication usually occurred following intravenous injections of diazepam in patients who were in a debilitated condition, or who had already received a variety of hypnotic agents. Several authors have warned against the injudicious use of the drug under such circumstances.¹⁸⁻²⁰ Respiratory depression was not encountered in any of our patients treated with continuous infusion of diazepam, all of whom had received multiple doses of anticonvulsants prior to institution of this mode of therapy. Also, all patients continued to receive 3 to 6 mg/Kg/day of phenobarbital in order to take advantage of synergistic potential.²¹ In point of fact, all four of our patients who had apneic episodes as accompaniments of their seizure activity resumed normal respiratory excursions as soon as seizures came under control. However, it must be emphasized that the tendency towards over-treatment in the emergency situation of status epilepticus is a real one, and early resort to diazepam by intravenous infusion in highly diluted form would obviate such risks. The present study indicates that diazepam administered by continuous intravenous infusion in order to maintain constant therapeutic levels is effective for the control of severe refractory convulsions, and successfully prevents their recurrence.

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References

1. EPSTEIN, M. H., O'CONNOR, J. S.: Destructive effects of prolonged status epilepticus. *J. Neurol. Neurosurg. Psychiat.*, 29:251-254, 1966.
2. SMITH, B. T., MASOTTI, R. E.: Intravenous diazepam in the treatment of prolonged seizures in neonates and infants. *Develop. Med. Child. Neurol.*, 13:630-634, 1971.
3. CALDERON-GONZALEZ, R., MIRALLES-GONZALEZ, A.: Management of prolonged motor seizure activity in children. *J. Amer. Med. Ass.*, 204:544-546, 1968.
4. GORDON, N. S.: Treatment of status epilepticus with diazepam. *Develop. Med. Child. Neurol.*, 8:668-672, 1966.
5. BAILEY, D. W., FENICHEL, G. M.: The treatment of prolonged seizure activity with intravenous diazepam. *J. Pediatr.*, 73:923-927, 1968.
6. MCMORRIS, S., MCWILLIAM, P. K. A.: Status epilepticus in infants and young children treated with parenteral diazepam. *Arch. Dis. Child.*, 44:604-611, 1969.
7. PARSONAGE, M. J., NORRIS, J. W.: Use of diazepam in treatment of severe convulsive status epilepticus. *Brit. Med. J.*, 3:85-88, 1967.
8. PRENSKY, A. L., RAFF, M. C., MOORE, M. J., SCHAW, R. S.: Intravenous diazepam in the treatment of prolonged seizure activity. *N. Engl. J. Med.*, 276:779-784, 1967.
9. LALJI, D., HOSKING, C. S., SUTHERLAND, E.: Diazepam in the control of status epilepticus. *Med. J. Aust.*, 1:542-545, 1967.
10. RANDALL, L. D., HEISE, G. A., SCHALLECK, W., BAGDON, R. E., BANZIGER, R., BORIS, A., MOE, R. A., ABRAMS, W. B.: Pharmacological and clinical studies of valium: A new therapeutic agent of the benzodiazepine class. *Curr. Therap. Res.*, 3:405-425, 1961.
11. FEMI-PEARSE, D., FLEMING, S. A.: Tetanus treated with high dosage of diazepam. *J. Trop. Med. Hyg.*, 68:305-306, 1965.
12. FEMI-PEARSE, D.: Experience with diazepam in tetanus. *Brit. Med. J.*, 2:862-865, 1966.
13. HENDRICKSE, R. G., SHERMAN, P. M.: Tetanus in childhood: report of a therapeutic trial of diazepam. *Brit. Med. J.*, 2:860-862, 1966.
14. GEDIOGLU, G., YALSIN, I., AYGEN, A., CAKIN, I.: Diazepam in tetanus. *Lancet*, 2:454, 1973.
15. GREWAL, R. S., SHARMA, B. K.: Valium in the treatment of tetanus. *Ind. Pract.*, 22:643-646, 1969.
16. GASTAUT, H., NAQUET, R., POIRE, R., TASSINARI, C. A.: Treatment of status epilepticus with diazepam. *Epilepsia*, 6:167-182, 1965.
17. MELKEBACK, A. VAN, DEBARSY, A. M.: "A propos d'un inconvenient rare, mais dramatique, de d'utilisation du diazepam intraveineux." *Acta Neurol. Belg.*, 70:286-294, 1970.
18. LOMBROSO, C.: Treatment of status epilepticus with diazepam. *Neurology*, 16:629-634, 1966.
19. SAWYER, G. T., WEBSTER, D. D., SCHUT, L. J.: Treatment of uncontrolled seizure activity with diazepam. *J. Amer. Med. Ass.*, 203:913-918, 1968.
20. BELL, D. S.: Dangers of treatment of status epilepticus with diazepam. *Brit. Med. J.*, 1:159-161, 1969.
21. FOURNADJEV, G., BOISEMARE, F., LECHAT, P.: "Activité comparée de diverses associations d'anticonvulsivants vis-à-vis de l'électrochoc chez la souris." *Thérapie*, 23:1363-1370, 1968.

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Actinomycosis Arthritis: A Case Report

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Abstract

Since its discovery nearly one hundred years ago, *Actinomyces israelii* has been implicated in infection of virtually every organ system. Bone involvement, except for the mandible, is uncommon, and disease in the long bones is rare. A previously well patient presenting with pain, swelling, and warmth of his right ankle was found to have actinomycosis arthritis.

Actinomycosis is a chronic, suppurative fungal infection caused by *Actinomyces israelii*. The organism was first recognized as the "ray fungus" by Harz and Bollinger in 1877 and was isolated from human necropsy material in the following year by Israel. Wolff and Israel associated it with human disease in 1891 when they isolated the organism in pure culture from a patient.^{1,2} Since that time *Actinomyces israelii* has been implicated in infections in many regions of the body; however, we found only scanty mention in the literature of atraumatic involvement of peripheral joints in an otherwise healthy individual. The following is a case report of actinomycosis arthritis involving the ankle and knee.

Case Report

The patient is a 47 year old, black, male statistician who developed pain in his right ankle 3½ months prior to admission. There was no history of trauma. The patient treated himself

with epsom salts and liniments. Two weeks after the onset of the pain, he noted mild swelling and warmth in the ankle and consulted an orthopedic surgeon, who treated him with intra-articular steroid injections and immobilization of the joint. Although he received four additional steroid injections during the next two months, the joint became more swollen and painful. Two weeks prior to admission, he was treated with 25 mg of Indocin three times a day without improvement.

The patient was admitted to the Washington, D.C. Veterans Administration Hospital on 10/27/72 for further evaluation of this problem. Other problems at this time included ischemic heart disease with a myocardial infarction in 1970, Type II hyperlipoproteinemia, and nerve deafness of unknown etiology in the left ear. There was no previous history of arthritis, trauma, fever, skin rashes, urethral discharge, or eye problems. The patient gave no history of tuberculosis and had had negative skin tests previously.

Physical examination revealed deafness in the left ear, bilateral arcus senilis, an atrial diastolic gallop, and a swollen, tender right ankle that was neither warm nor erythematous. Oral hygiene was good, the patient was afebrile, and the chest x-ray was within normal limits. ECG showed lateral wall ischemic changes. X-ray of the right ankle showed soft tissue swelling and demineralization of the tarsal bones. The hematocrit was 47,

wbc 6,800 with 61 neutrophils, 35 lymphocytes, and 4 monocytes. Uric acid on three occasions was 8.0, 7.3, and 7.4 mg%. The sedimentation rate was 10 mm/hr. Lupus erythematosus preps were negative on two occasions and rheumatoid arthritis latex fixation was weakly reactive. Skin testing for tuberculosis with intermediate strength PPD was positive. On 11/3/72 an open biopsy of the synovium, talus, and fibula of the right ankle was performed.

Histologic examination of the synovium demonstrated only nonspecific inflammatory changes and the bone was unremarkable. Bacterial and tuberculosis cultures were negative; however, on anaerobic culture the synovium grew *Actinomyces israelii*.

While awaiting the culture results the patient was discharged on Indocin 50 mg tid and one day later experienced the onset of pain, swelling and warmth in the right knee. This became progressively worse, to the point that he was unable to walk, and eight days after discharge he was started on potassium penicillin VK 500 mg po q6h. When the patient failed to improve, he was readmitted on 11/24/72 and the penicillin was discontinued. Physical examination was unchanged except for a Grade II/VI systolic ejection murmur along the left sternal border, and the right knee which was warm, tender and swollen. Chest X-ray was again normal, and films of the right ankle were unchanged. X-rays of the right knee demonstrated patchy demineralization of the femoral con-

dyles and patella. The ECG was unchanged.

Three days after the penicillin was discontinued, six blood cultures were obtained and arthrocentesis of the right knee was performed. The patient was then started on aqueous penicillin G five million units IV q6h. Blood and joint fluid cultures were negative for bacteria, fungi, and tuberculosis. During a three week course of 20 million units of IV penicillin daily the patient showed gradual disappearance of symptoms and joint findings, and the heart murmur was unchanged. X-rays of the right knee initially showed worsening of the demineralization, but this had stabilized prior to discharge, and the patient left the hospital in good condition on potassium penicillin VK 500 mg po q6h.

Discussion

Actinomyces israelii is an anaerobic or microaerophilic gram positive branching filamentous fungus which is a normal inhabitant of carious teeth, the gingiva, and tonsillar crypts.²⁻⁷ The organism is a harmless saprophyte in these locations but may be swallowed and traverse the alimentary tract, may be inhaled or aspirated into the lungs, may extend into the jaw following local trauma,^{2,7,8} and may rarely enter by way of the female genital tract.⁹ The actinomycete cannot penetrate intact epithelium unless there is some local traumatic or pathologic lesion, but given the opportunity it can grow and spread widely in the connective tissue.^{2,7,10}

Cope in 1938 published the largest series of actinomycosis infections, describing 1330 cases,^{2,4,11} and grouping the disease into three main categories: cervicofacial (63%), abdominal (22%), and thoracic (15%). Involvement of the skull and epidural space,¹¹ maxilla,⁵ mandible,² tongue,¹² thyroid,^{2,13} breast,¹⁴ heart, lungs, mediastinum, and

chest wall,^{1,6,9,13,15} esophagus,¹⁵ liver,^{9,16} pancreas,¹⁷ intestines,^{2,9} transverse mesocolon,¹⁸ kidneys,¹⁹ female reproductive organs,⁹ and anorectum²⁰ have been described.

While bone, particularly the mandible,⁵ is not exempt from the ravages of actinomycosis, skeletal involvement is not common.^{7,8,20} Bone disease may arise from primary infection, which chiefly affects the lower jaw,² spread from neighboring disease,^{2,7,8,20} and metastatic spread.^{2,3,5,13,18} Actinomycosis spondylitis is a relatively "common" location of osseous involvement, but thus far only seventy cases have been described.^{7,8,21}

Involvement of the extremities is even less common, with fewer than a dozen reported cases prior to 1951.⁷ Since that time we have been able to find only nine additional cases.^{10,13,22,23} Most of these reported cases were secondary to infections in the adjacent soft tissues,^{10,21} dissemination from distant sites,¹³ trauma,¹⁰ or human bites.^{2,24} We were able to find but one prior case of atraumatic synovial joint involvement in a previously well patient.²⁵

The pathogenesis of the actinomycosis arthritis in the present case report remains speculative. Oral hygiene was good, and there was no antecedent dental manipulation, trauma or infection. The chest X-ray was clear, there were no respiratory or gastrointestinal symptoms, the soft tissues of the right leg were free from involvement, and there was no trauma involving the leg. Hematogenous spread is said to be uncommon,^{3,19} but has nevertheless been described.^{2,5,13} Cope, furthermore, raises the possibility of the primary site of infection disappearing, leaving only the metastatic lesions.²

The occurrence of both ankle and knee involvement in the present case makes the possibility of blood-borne infection an attractive hypothesis. The

knee may have been involved secondary to hematogenous spread from the ankle, or both joints may have been infected secondary to an unfound primary lesion. Extension by the blood stream is most common when the lung is the site of the primary disease,² but history, physical, and roentgenograms revealed no pulmonary pathology. The presence of a heart murmur raised the question of actinomycotic endocarditis¹⁵ giving rise to hematogenous spread, but there was no other evidence of embolic phenomena, the patient was afebrile, there was no leukocytosis, and anaerobic blood cultures were negative.

While there is a report of actinomycosis introduced by a hypodermic needle,¹⁰ our patient clearly had joint symptoms before undergoing steroid injections of his ankle.

Certain similarities to tuberculous arthritis exist,²⁶ and indeed this was the tentative diagnosis in our patient prior to culture reports. Although extremely rare, actinomycosis arthritis might, therefore, be considered when patients present with a picture consistent with tuberculous arthritis.

Summary

A brief survey of the literature on human actinomycosis, with special reference to bone involvement, is presented, and a rare case of actinomycosis arthritis is reported.

The patient is a 47 year old black male who entered with pain, swelling, and warmth in his right ankle and was found to have actinomycosis on anaerobic culture of the synovium. Subsequently, the patient was readmitted for similar complaints in the right knee. High dose, long term penicillin therapy was started and the patient responded well.

ACTINOMYCOSIS ARTHRITIS

SHERER AND DOBBINS

References

1. PRATHER, J. R., EASTRIDGE, C. E., HUGHES, E. A., et al: Actinomycosis of the Thorax. *Ann. Thor. Surg.*, 1970, 9, 307.
2. COPE, V. Z.: Actinomycosis. London, Oxford U. Press, 1938.
3. ADAR, R., ANTEBI, E., DAVID, R., et al: Abdominal Actinomycosis. *Israel J. Med. Sci.*, 1972, 8, 148.
4. COPE, V. Z.: Actinomycosis. *Practitioner*, 1939, 142, 319.
5. GOLDSTEIN, B. H., SCIUBBA, J. J., LASKIN, D. M.: Actinomycosis of the Maxilla. *J. Oral Surg.*, 1972, 30, 362.
6. TOMM, K. E., RALEIGH, J. W., GUINN, G. A.: Thoracic Actinomycosis. *Am. J. Surg.*, 1972, 124, 46.
7. COPE, V. Z.: Actinomycosis of Bone with Special Reference to Infection of the Vertebral Column. *J. Bone and Joint Surg.*, 1951, 33B, 205.
8. ERNST, J., RATJEN, E.: Actinomycosis of the Spine. *Acta. Orthop. Scand.*, 1971, 42, 35.
9. CAMPBELL, D. A., BRADFORD, B.: Actinomycosis of the Thorax and Abdomen. *Arch. Surg.*, 1948, 57, 202.
10. CULLEN, C. H., SHARP, M. E.: Infection of Wounds with Actinomyces. *J. Bone and Joint Surg.*, 1951, 33B, 221.
11. KIRSCH, W. M., STEARS, J. C.: Actinomycotic Osteomyelitis of the Skull and Epidural Space. *J. Neurosurg.*, 1970, 33, 347.
12. UHLER, I. V., DOLAN, L. A.: Actinomycosis of the Tongue. *Oral Surgery*, 1972, 34, 199.
13. BUTAS, C. A., READ, S. E., COLEMAN, R. E., et al: Disseminated Actinomycosis. *Can. Med. Assoc. J.*, 1970, 103, 1069.
14. GOGAS, J., SECHAS, M., DIAMANTIS, S., et al: Actinomycosis of the Breast. *Int. Surg.*, 1972, 57, 664.
15. DUTTON, W. P., INCLAN, A. P.: Cardiac Actinomycosis. *Dis. Chest*, 1968, 54, 65.
16. YAMADA, T., SAKAI, A., TONOUCHI, S., et al: Actinomycosis of the Liver. *Am. J. Surg.*, 1971, 121, 341.
17. SERRANO-RIOS, M., NAVARRO, V., FONTAN, J., et al: Isolated Hepato-Pancreatic Actinomycosis. *Digestion*, 1969, 2, 262.
18. MILLER, R. E., KATZ, S.: Actinomycosis of the Transverse Mesocolon. *Am. J. Surg.*, 1971, 122, 414.
19. ANHALT, M., SCOTT, R.: Primary Unilateral Renal Actinomycosis. *J. Urol.*, 1970, 103, 126.
20. SAMENIUS, B.: Actinomycosis of the Anorectal Region. *Proc. R. Soc. Med.*, 1970, Suppl. 63, 108.
21. BRETT, M. S.: Advanced Actinomycosis of the Spine Treated with Penicillin and Streptomycin. *J. Bone and Joint Surg.*, 1951, 33B, 215.
22. MARTINELLI, B., TAGLIAPIETRA, E. A.: Actinomycosis of the Arm. *Bull. Hosp. Joint Dis.*, 1970, 31, 31.
23. ALTEMEIER, W. A., LARGEN, T.: Antibiotic and Chemotherapeutic Agents in Infections of the Skeletal System. *J.A.M.A.*, 1952, 150, 1463.
24. WILLIAMS, C. A.: Actinomycosis of Phalanx of Finger. *Ann. Surg.*, 1917, 66, 117.
25. ALLENBACH, R.: cited by Cope, ref. 2.
26. BERNEY, S., GOLDSTEIN, M., BISHKO, F.: Clinical and Diagnostic Features of Tuberculous Arthritis. *Am. J. Med.*, 1972, 53, 36.

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The Use of Immunosuppressive Agents in Takayasu's Arteritis *

HUBERT J. ALPERT, M.D.

Abstract

A 54-year-old woman presented with Takayasu's arteritis preceded by a prepulseless phase of 16 years duration. Prednisone therapy resulted in numerous side effects and did not halt the progression of disease. The addition of azathioprine and, later, cyclophosphamide resulted in clinical improvement and enabled the patient to reduce the prednisone dosage. This case study is the first report of immunosuppressive agents in the treatment of Takayasu's arteritis.

Introduction

Takayasu's arteritis is an inflammatory disease of the larger arteries, usually involving the aortic arch and its branches¹. Although the etiology is unknown, an autoimmune process has been postulated^{2,3}. A search of the literature revealed no reports with immunosuppressive agents in the treatment of this disease, although this approach has been suggested by several investigators^{4,5}.

Case Report

D.H., a 54-year-old white woman was admitted to the Washington Hospital Center with fever and upper extremity weakness and cramping.

Sixteen years before admission she developed proximal interphalangeal

joint arthralgias controlled with chronic aspirin ingestion. Two years prior to admission, pain in the cervical spine, shoulders, hips, and knees ensued, followed by arthritis of the left knee. At that time, evaluation revealed a swollen, tender left knee; a positive rheumatoid factor; a sedimentation rate of 33 mm per hour; hemoglobin, 11.8 g per 100 ml; hematocrit, 37 volumes per 100 ml; creatinine clearance, 63 ml per minute; and X-rays showing minimal to modest degenerative arthritis. The blood pressure, serum creatinine, BUN, IVP, and urinalysis were all normal.

The patient was admitted to the Washington Hospital Center in April, 1969, at age 54, with fever to 39°C of two weeks duration. Her arthralgias had been minimal just prior to admission, but she had weakness of the upper extremities, and forearm cramping. The blood pressures six months previously were 160/100 mm Hg in the right arm, 162/104 mm Hg in the left arm. These elevated readings were subsequently normal without specific medication. The last blood pressure reading, three months prior to admission, was 140/80 mm Hg. Myalgia and muscle tenderness were not present.

Physical examination revealed a blood pressure in the left arm of 85/60 mm Hg and a systolic pressure in the right arm at 30 mm Hg, to palpation only. Systolic blood pressure in the legs was 160 mm Hg. There was slight

A/V nicking on fundoscopic exam but no hemorrhages or "rosettes". Bruits were audible in both axillae, over the scapular areas, in the epigastrium and left carotid and right iliac arteries. There were no trophic changes of the skin, nails, or subcutaneous tissue. The joints appeared normal except for the chronic changes in the left knee.

The hematocrit was 32; hemoglobin 9.7 g per 100 ml; platelet count, 800,000 per mm³; sedimentation rate, 36 mm per hour; and white count, 10,000 per mm³ with a slight left shift. The gamma globulins were normal; the alpha₂ globulins were elevated to 1.25 g per 100 ml. The serum iron was 32 mcg per 100 ml, iron-binding capacity was 231 mcg per 100 ml, and bone marrow exam revealed decreased iron stores. The creatinine clearance was 60 ml per minute, but again urinalysis, blood urea nitrogen, and creatinine were normal, as were lipid studies, lupus erythematosus preparations, antinuclear antibodies, and serology.

Angiography was done through a femoral approach. Both subclavian arteries were narrowed markedly with maximal narrowing at the axillary arteries. Abundant collateral vessels were noted. The aorta, carotids, vertebral, innominate, celiac axis, renal, superior and inferior mesenteric, and iliac vessels all appeared normal.

The patient was treated with prednisone, 60 mg daily, and ferrous

IMMUNOSUPPRESSIVE AGENTS IN TAKAYASU'S ARTERITIS

ALPERT



FIG. 1: The angiogram shows maximal narrowing of the axillary artery and abundant collateral vessels.

fumarate. The anemia, fever, and thrombocytosis abated promptly. The pulses, however, continued to diminish, and the patient developed rapid weight gain, hypertension, Cushingoid features, and diabetes secondary to the steroids. Reduction in steroid dosage or alternate-day steroid regimen caused a recurrence of systemic symptoms.

Four months after discharge, azathioprine, 150 mg to 200 mg daily, was added. One and one-half years later, cyclophosphamide, 100 mg to 125 mg daily, was substituted. The use of immunosuppressant agents enabled the patient to reduce the steroids and to switch to an alternate-day schedule.

Currently (1973), she is taking

prednisone, 30 mg every other day. The cyclophosphamide was recently discontinued. The disease is not nearly as active, and the current levels of medication were not possible even one year ago. A recent blood pressure in the left arm was 120/80 mm Hg; the right brachial pulse remains barely palpable.

During the last four years, the patient had a right retinal vein occlusion with hemorrhage and subsequent glaucoma. She developed bilateral cataracts followed by a successful left cataract extraction.

Discussion

Biopsy confirmation of Takayasu's

arteritis has not been obtained; but the angiograms left little doubt of the diagnosis⁶. Although this woman was older than most with Takayasu's arteritis, case reports of people above 50 years of age are by no means rare^{7,8}. Arteriosclerosis, syphilis¹, and giant cell arteritis³ were also considered. Giant cell arteritis can occasionally cause an aortic arch syndrome, making the clinical and even the histologic diagnosis indistinguishable from Takayasu's^{9,10}. However, the onset of rheumatic symptoms at age 38 without symptoms of polymyalgia rheumatica makes a diagnosis of Takayasu's arteritis more likely than giant cell arteritis.

Patients with Takayasu's arteritis usually have prolonged systemic symptoms suggestive of autoimmune disease¹¹. It has been associated with systemic lupus erythematosus, rheumatoid arthritis, polymyositis, and ankylosing spondylitis¹²⁻¹⁴. Antiaortic antibodies have been looked for without success^{2,15,16}.

Although corticosteroids have had wide use in this disease, there is a lack of any reasonable alternative. The similarity of Takayasu's arteritis with other immune complex disease led to the use of immunosuppressants based on successful trials in rheumatoid arthritis¹⁷. In this disease, there is serologic improvement as well as clinical benefit.

The mechanism of action of cytotoxic drugs in immune complex disease is obscure¹⁸. These drugs suppress antibody production, inhibit cellular immunity, and reduce inflammation. In low doses, as in this case, the immunosuppressive drugs probably act primarily as anti-inflammatory agents.

The patient was switched to cyclophosphamide in late 1970 because of advances in therapy¹⁷ rather than the patient's unresponsiveness to azathioprine. The immunosuppressive agents enabled the patient to reduce the

steroids which were disabling when used alone at the increased dosage. At the present time, the patient has reached a quiescent phase and no longer requires immunosuppressant agents.

Summary

A case summary of a patient with Takayasu's arteritis is presented. This report documents, for the first time, improvement with the use of immunosuppressive agents.

Acknowledgments

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References

1. ROSS, R. S., McKUSICK, V.: Aortic arch syndrome. Diminished or absent pulses in arteries arising from arch of aorta. *A.M.A. Arch. Int. Med.* 92:701, 1953.
2. STRACHAN, R. W., WIGZELL, F. W., ANDERSON, J. R.: Locomotor manifestations and serum studies in Takayasu's arteriopathy. *Amer. J. Med.* 40:560, 1966.
3. EDITORIAL: Arteritis of the aorta and its branches. *Lancet* 1:642, 1965.
4. STRACHAN, R. W.: Pre-pulseless and pulseless Takayasu's arteritis. *Postgrad. Med. J.* 42:464, 1966.
5. HELD, K., JIPP, P.: Diagnosis, etiology and treatment of the aortic arch syndromes. *Med. Klin.* 65:845, 1970.
6. GROLLMAN, J. H., HANAFAER, W.: The Roentgen diagnosis of Takayasu's arteritis. *Radiology* 83:387, 1964.
7. SANDRING, H., WELIN, G.: Aortic arch syndrome with special reference to rheumatoid arthritis. *Acta Med. Scand.* 170:1, 1961.
8. ASK-UPMARK, E.: On the pulseless disease outside of Japan. *Acta Med. Scand.* 149:161, 1954.
9. HAMILTON, C. R., SHELLY, W. M., TUMULTY, P. A.: Giant cell arteritis. *Medicine* 50:1, 1971.
10. HUNDER, G. G., WARD, L. E., BURBANK, M. D.: Giant cell arteritis producing an aortic arch syndrome. *Ann. Int. Med.* 66:578, 1967.
11. STRACHAN, R. W.: The natural history of Takayasu's arteriopathy. *Quart. J. Med.* 33:57, 1964.
12. PALOHEIMA, J. A.: Obstructive arteritis of Takayasu's type. *Acta Med. Scand. Suppl.* 468, 1967.
13. LESSOF, M. H., GLENN, L. E.: The pulseless syndrome. *Lancet* 1:799, 1959.
14. FALICOV, R. E., COONEY, D. F.: Takayasu's arteritis and rheumatoid arthritis. *Arch. Int. Med.* 114:594, 1964.
15. HIRSCH, M. S., AIKAT, B. K., BASU, A. K.: Takayasu's arteritis. *Bull. Johns Hopkins Hosp.* 115:29, 1964.
16. ASHERSON, R. A., ASHERSON, G. L., SCHRIRE, V.: Immunological studies in arteritis of the aorta and great vessels. *Brit. Med. J.* 3:589, 1968.
17. COOPERATING CLINICS COMMITTEE OF THE AMERICAN RHEUMATISM ASSOCIATION: A controlled trial of cyclophosphamide in rheumatoid arthritis. *New England J. Med.* 283:883, 1970.
18. STEINBERG, A. D., et al.: Cytotoxic drugs in treatment of nonmalignant diseases. *Ann. Int. Med.* 76:619, 1972.

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Sympathetic Beta Adrenergic Blockade in the Preoperative Treatment of Hyperthyroidism

ARNOLD G. BRODY, M.D. AND ROBERT DIBBLE, M.D.

The physician treating a patient with hyperthyroidism may elect to use either radioactive iodine, the antithyroid drugs propylthiouracil or methimazole, or surgery. Toxic reactions have been reported to occur in 6% to 45% of patients receiving antithyroid drugs.^{1,2} Some of these side effects such as agranulocytosis, jaundice, or severe sensitivity reactions including rheumatoid-like arthritis or vasculitis, constitute absolute indications for discontinuing the drug.³ At this point, the physician must change to either surgery or radioactive iodine therapy. In patients under 23 years of age, a predisposition to develop thyroid nodules or thyroid carcinoma after exposure of the thyroid gland to radiation has been reported.⁴ Therefore, at the present time, surgery is the treatment of choice in this age group.

In the pre-operative management of patients who are hyperthyroid, the patient is usually treated with antithyroid drugs and iodine. However, if a serious toxic reaction to antithyroid drugs has already occurred, one would not want to risk exposing the patient to the drug again. Fortunately, in recent years, sympathetic blocking drugs such as guanethidine and propranolol have been useful in treating thyrotoxicosis.^{5,6,7,8,9} There have been limited reports on the use of propranolol in the preoperative management of hyperthyroidism, including its use in patients who have had

antithyroid drugs discontinued because of toxic reactions.^{8,9,10} We are reporting our experience with a patient in whom thyroidectomy was successfully performed after pre-operative treatment with propranolol and iodine. Propylthiouracil had previously been discontinued when jaundice developed.

Case Report

This 18 year old girl was seen by her family physician in March, 1971. She complained of nervousness for one year, weight loss from 135 to 117 lbs. during the previous month, sweating of the palms and enlargement of her eyes. There was no insomnia. She had one normal pregnancy with delivery of a normal infant in 1970.

Her physician noted that the patient had a diffusely enlarged goitre, made the diagnosis of hyperthyroidism, and started the patient on Propylthiouracil. Ten days after she began taking Propylthiouracil she became jaundiced. Propylthiouracil was stopped and she was admitted to the hospital on April 14, 1971.

Physical examination revealed a thin, very hyperactive young woman. The B.P. was 140/68 and the pulse was 130 per minute. She had bilateral lid lag and exophthalmos. The sclerae were icteric. The thyroid was diffusely enlarged two times the normal size. No bruits were heard over the gland. A

fine tremor was present. The liver was palpable 2 cm below the right costal margin and non-tender. Lab data one week before admission to the hospital showed a bilirubin of 4 mg% and a serum glutamic oxaloacetic transaminase (SGOT) of 200 units. Follow up studies after admission to the hospital showed a fall of the bilirubin to 2.7 and later 1.25 mg%; the SGOT fell to 150 and later to 50 units. Serum glutamic pyruvic transaminase was 44 units, and the alkaline phosphatase fell from 150 units to 110 units (N = 30-80). The protein bound iodine was 14.5 mcg%, the T4 was 16 mcg% (N = 4-11) and the T3 uptake 16.2% (N = 11-18%). Thyroid scan showed diffuse enlargement. I₁₃₁ uptake at 24 hours was 69.6%. The complete blood count, urinalysis, chest X-ray, skull X-ray, and upper gastrointestinal X-rays were within normal limits.

On April 15 Guanethidine 25 mg three times daily was started. Three days later, the pulse was 88 per minute, the blood pressure was 110/80 and the nervousness, sweating, and tremor were markedly improved. Because of the patient's age, we were reluctant to treat her with radioactive iodine and surgery was planned. On April 28, Guanethidine was stopped and Propranolol 20 mg every six hours was started, in addition to Lugol's solution five drops three times daily. The patient's clinical condition re-

mained stable as before. On May 7, a sub-total thyroidectomy was performed. The patient tolerated surgery well. Her post-operative course was uneventful except for transient post-operative tetany and hypocalcemia which responded to Vitamin D and calcium. Propranolol was stopped four days after surgery and the patient did not experience any symptoms of hyperthyroidism. The microscopic examination showed a nodular colloid goitre with areas of increased activity.

Discussion

A small percentage of patients taking propylthiouracil or methimazole have been reported to develop toxic reactions. A report by Amrhein *et al*², in which 45% of the patients had a toxic reaction and 18% had granulocytopenia, suggests that these side effects may occur more often than was previously suspected. Most of these drug reactions, such as skin rash or fever, are not serious. When they occur the physician may try changing from one anti-thyroid drug to another, for example, from Propylthiouracil to methimazole, as the second drug may not cause toxicity in that patient. On the other hand, when serious reactions such as agranulocytosis or jaundice occur the drug must be stopped immediately. The physician may not wish to try another antithyroid drug for fear that a similar serious reaction may occur again. The patient whom we have reported developed liver disease and jaundice and we did not want to risk further hepatic toxicity by using another antithyroid drug. Therefore we were left with a choice of surgery or radioactive iodine for treating her hyperthyroidism.

In an older patient, who could not have pre-operative preparation with antithyroid drugs prior to surgery, radioactive iodine would be the treatment of choice. However, the reports of thyroid nodules and thyroid carci-

noma occurring in young people whose thyroid glands have been exposed to ionizing radiation, made us reluctant to use radioactive iodine in this girl. In addition, there are the possible risks of leukemia developing many years later, and of genetic problems secondary to irradiation of the reproductive organs after radioactive iodine. Furthermore, there is the risk of hypothyroidism occurring later in life after radioactive treatment, a risk that increases with the length of time that patients are followed¹¹. Therefore we elected to treat our patient with thyroidectomy.

Thyroidectomy has been shown to be a precipitating factor in provoking thyrotoxic crisis (thyroid storm) in patients who were not treated pre-operatively with antithyroid drugs¹². In view of the reports of sympathetic blocking drugs being useful in treating hyperthyroidism we felt that their pre-operative use in addition to iodine would be beneficial in preparing this patient for surgery. Of the drugs guanethidine and propranolol, guanethidine had some disadvantages. It has a slow onset, a long duration of action, and there are hypotensive complications. We therefore elected to use propranolol because with its more rapid onset of action, and shorter duration of action, the patient can be more easily monitored.

Propranolol acts by blocking the beta receptors of the sympathetic nervous system. It has been shown to be effective in improving the cardiovascular abnormalities of hyperthyroidism^{6,7}. Vinik⁸ reported on the use of propranolol in hyperthyroid patients (including some patients undergoing thyroidectomy). They recommended its use in preparing patients for thyroidectomy in conjunction with iodine in (1) patients who had reactions to other anti-thyroid drugs; (2) in shortening the pre-operative preparation time for surgery for patients from distant towns; and (3) in patients

still hyperthyroid after treatment with antithyroid drugs and iodine. In addition, they recommended its use in conjunction with treatment with radioactive iodine either before or after treatment for prompt control of symptoms, and while awaiting the results of diagnostic tests as it does not interfere with the PBI or I₁₃₁ tests of thyroid function.

Shanks *et al*⁹ reported that the use of propranolol and iodine in the preparation of hyperthyroid patients for surgery reduced the time needed to get the patient ready for surgery. They reported that the gland was less vascular and the operation technically easier than in patients prepared with antithyroid drugs.

Becker¹⁰ reported on three patients treated pre-operatively with propranolol. They had discontinued antithyroid drugs because of toxic reactions including agranulocytosis, granulocytopenia and thrombocytopenia, and pruritic skin eruption. They also noted that the post-operative course was uneventful and commented on the reduced vascularity of the thyroid gland which made the surgical procedure technically simpler.

Our experience was similar to those reported. There were no operative or post-operative complications related to the hyperthyroidism. It appears that propranolol is an acceptable alternative form of therapy in the pre-operative preparation of patients who have had toxic reactions to propylthiouracil and methimazole. Whether propranolol should be used in place of these antithyroid drugs or in addition to these antithyroid drugs in patients who have not had toxic reactions is not known at this time. Further studies will be necessary to answer these questions.

References

1. MCCLINTOCK, J. C., GASSNER, F. X., BIGELOW, N., BAKER, D. A.:

SYMPATHETIC BLOCKADE IN PREOPERATIVE HYPERTHYROIDISM

BRODY AND DIBBLE

- Antithyroid drugs in the treatment of hyperthyroidism. *Surg. Gynec. Obstet.*, 112:653-58, 1961.
2. AMRHEIN, J. A., KENNY, F. M., FREDERICK, M., ROSS, D.: Granulocytopenia, Lupus Like Syndrome and other complications of propylthiouracil therapy. *J. of Pediatrics*, v. 76, p. 54-63, 1970.
3. WERNER, S. D., INGBAN, S. H.: *The Thyroid*, 3rd Ed., 1971, p. 689.
4. HEMPELMAN, L. H.: Risk of thyroid neoplasms after irradiation in childhood. *Science*, v. 160, p. 159-63, 1968.
5. WALDSTIEN, S. S., WEST, G. H., LEE, W. U., BRONSKY, D.: Guanethidine in hyperthyroidism, *JAMA* 189:609-12, 1964.
6. TURNER, P., GRANVILLE-GROSSMAN, K. I., SMART, J. V.: Effect of adrenergic receptor blockade on the tachycardia of thyrotoxicosis and anxiety state, *Lancet* 2:1316-18, 1965.
7. HOWITT, G., ROWLANDS, D. J.: Beta Sympathetic Blockade in hyperthyroidism, *Lancet* 1:628-31, 1966.
8. VINIK, A. I., PIMSTON, B. L., HOFFENBERG, R.: Sympathetic blockade in hyperthyroidism, *J. Clin. Endocr.*, 28:725-28, 1968.
9. SHANKS, R. G., HADDON, D. R., LOWE, D. C., MCDEVITT, D. G., MONTGOMERY, D. A. D.: Controlled Trial of Propranolol in Thyrotoxicosis. *Lancet* 1:993-94, 1969.
10. BECKER, F. O., SCHWARTZ, T. B.: Sympathetic Blockade in Hyperthyroidism. *Arch. Int. Med.*, 129:967-71, 1972.
11. HAGEN, G. A.: Treatment of Thyrotoxicosis with I_{131} and Post Therapy Hypothyroidism, *Med. Clin. N. Amer.*, 52:417-29, 1968.
12. MCARTHUR, J. W., RAWSON, R. W., MEANS, J. H., COPE, O.: Thyrotoxic Crisis. *JAMA* 134:868-74, 1949.

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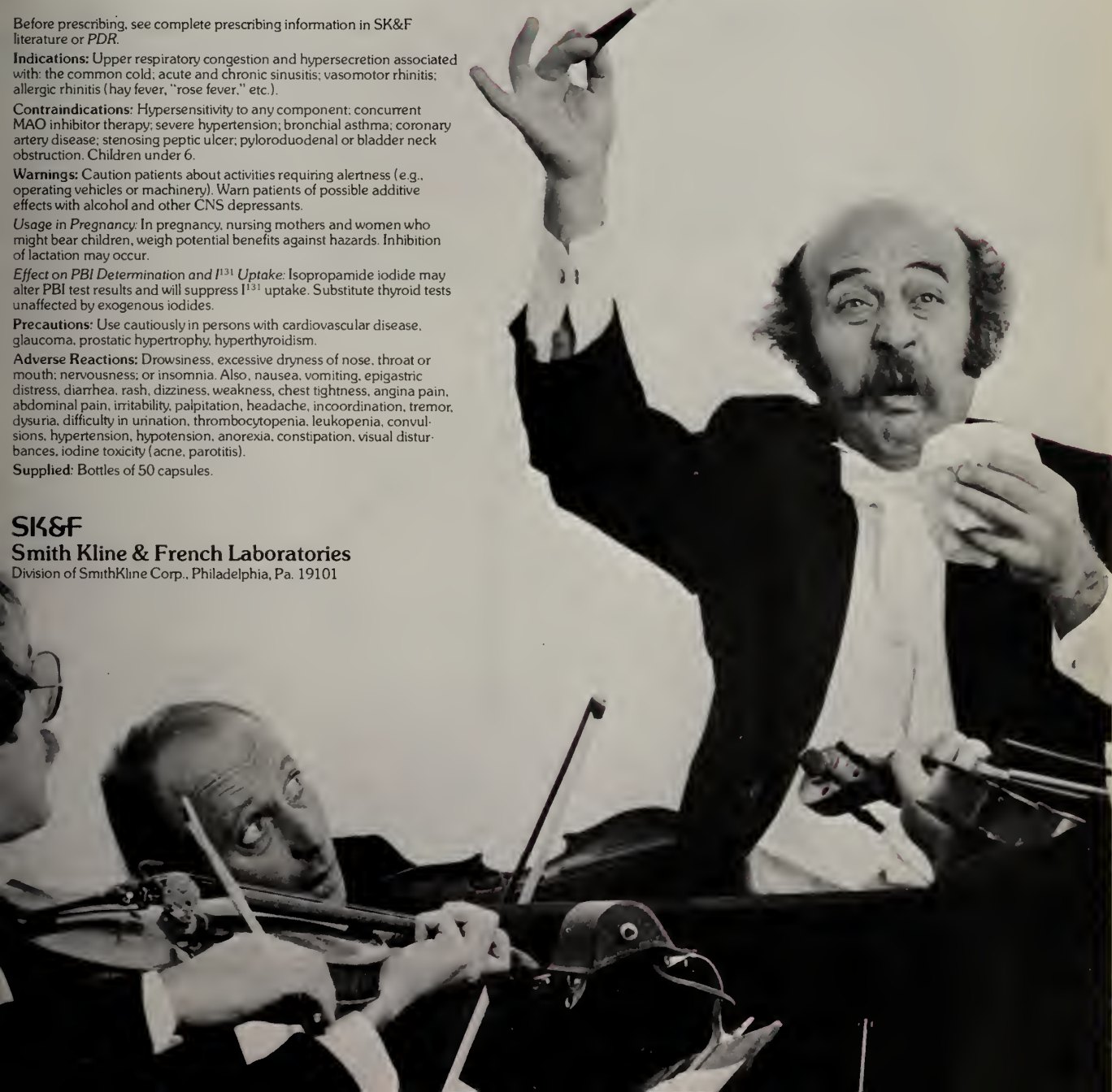
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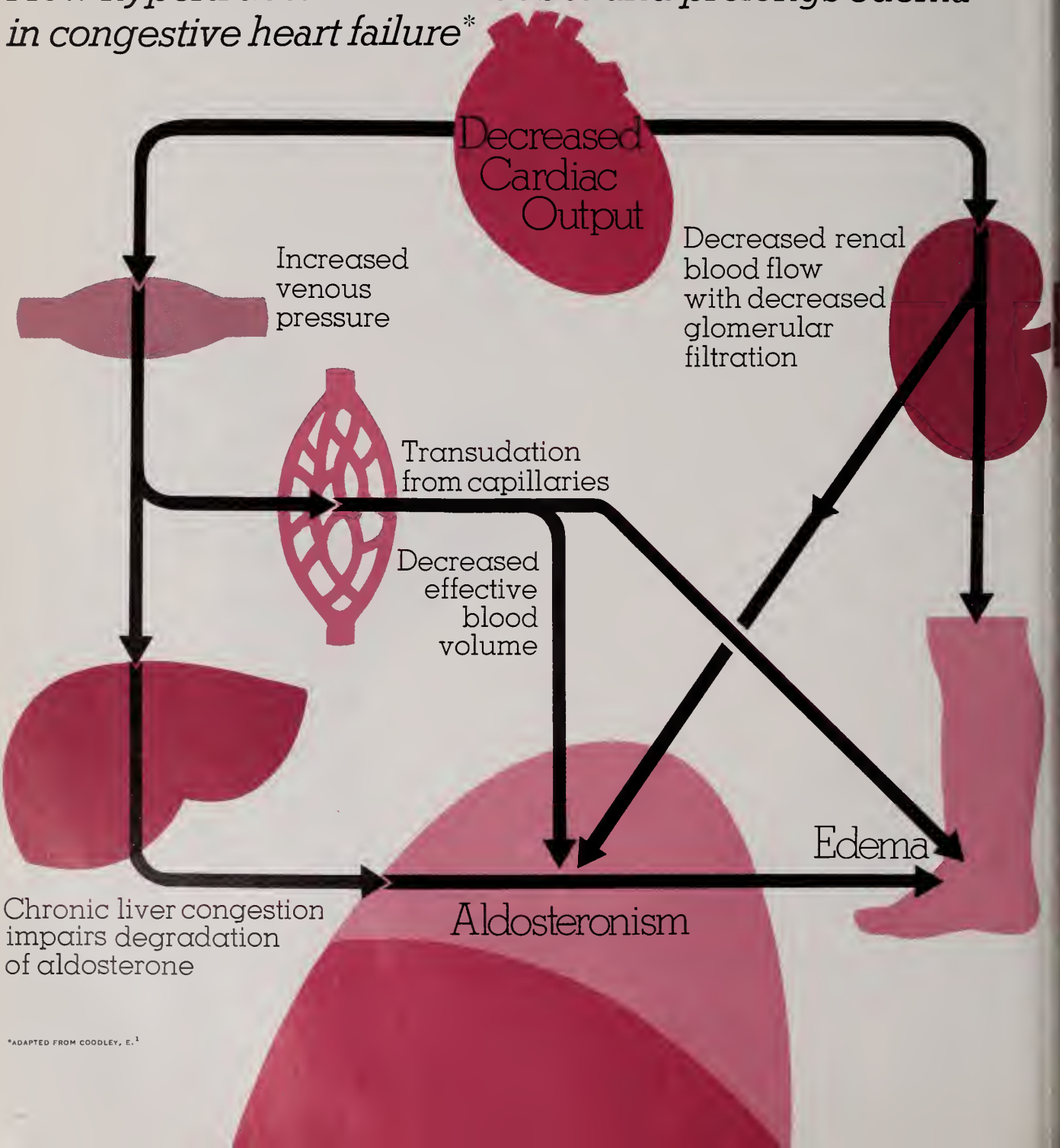
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Contraindications—Acute renal insufficiency, rapidly progressing impairment of renal function, anuria and hyperkalemia.

Warnings—Potassium supplementation may cause hyperkalemia and is not indicated unless a glucocorticoid is also given. Discontinue potassium supplementation if hyperkalemia develops. **Usage of any drug in women of childbearing age requires that the potential benefits of the drug be weighed against its possible hazards to the mother and fetus.**

Precautions—Patients should be checked carefully since electrolyte imbalance may occur. Although usually insignificant, hyperkalemia may be serious when renal impairment exists; deaths have occurred. Hyponatremia, manifested by dryness of the mouth, thirst, lethargy and drowsiness, together with a low serum sodium may be caused or aggravated, especially when Aldactone is combined with other diuretics. Elevation of BUN may occur, especially when pretreatment hyperazotemia exists. Mild acidosis may occur. Reduce the dosage of other antihypertensive drugs, particularly the ganglionic blocking agents, by at least 50 percent when adding Aldactone since it may potentiate their action.

Adverse Reactions—Drowsiness, lethargy, headache, diarrhea and other gastrointestinal symptoms, maculopapular or erythematous cutaneous eruptions, urticaria, mental confusion, drug fever, otaxia, gynecomastia, inability to achieve or maintain erection, mild androgenic effects, including hirsutism, irregular menses and deepening voice. Adverse reactions are infrequent and usually reversible.

Dosage and Administration—For essential hypertension in adults the daily dosage is 50 to 100 mg. in divided doses. Aldactone may be combined with a thiazide diuretic if necessary. Continue treatment for two weeks or longer since an adequate response may not occur sooner. Adjust subsequent dosage according to response of patient.

For edema, ascites or effusions in adults initial daily dosage is 100 mg. in divided doses. Continue medication for at least five days to determine diuretic response; add a thiazide or organic mercurial if adequate diuretic response has not occurred. Aldactone dosage should not be changed when other therapy is added. A daily dosage of Aldactone considerably greater than 75 mg. may be given if necessary.

A glucocorticoid, such as 15 to 20 mg. of prednisone daily, may be desirable for patients with extremely resistant edema which does not respond adequately to Aldactone and a conventional diuretic. Observe the usual precautions applicable to glucocorticoid therapy; supplemental potassium will usually be necessary. Such patients frequently have an associated hyponatremia—restriction of fluid intake to 1 liter per day or administration of mannitol or urea may be necessary (these measures are contraindicated in patients with uremia or severely impaired renal function). Mannitol is contraindicated in patients with congestive heart failure, and urea is contraindicated with a history or signs of hepatic coma unless the patient is receiving antibiotics orally to "sterilize" the gastrointestinal tract.

Glucocorticoids should probably be given first to patients with nephrosis since Aldactone, although useful for diuresis, will not directly affect the basic pathologic process.

For children the daily dosage should provide 1.5 mg. of Aldactone per pound of body weight.

References: 1. Coodley, E.: Consultant 12:106-107, 109, 111, 113, 115 (July) 1972. 2. Thorn, G. W., and Louler, D. P.: Am. J. Med. 53:673-684 (Nov.) 1972.

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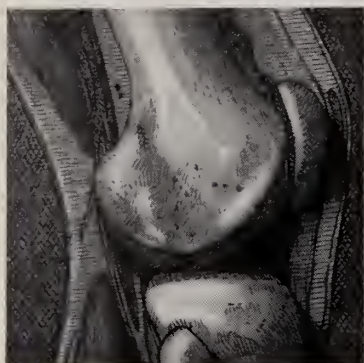
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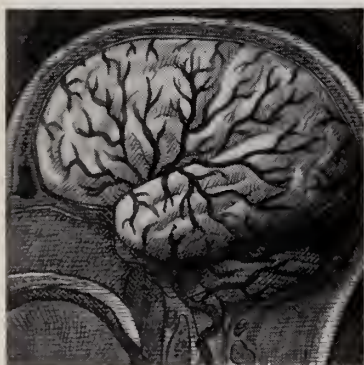
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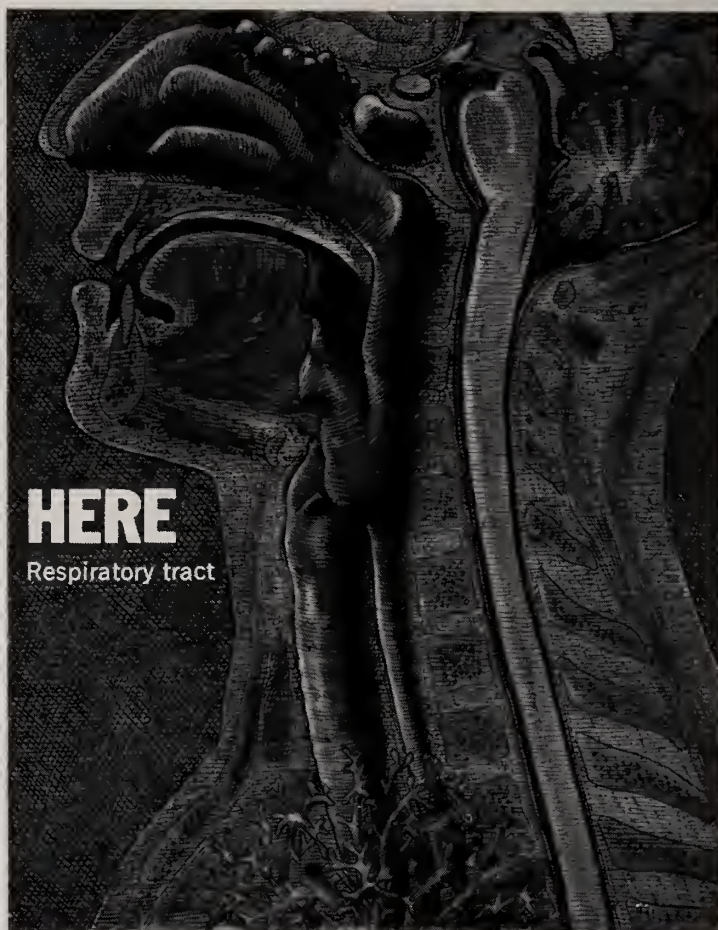
In flu and associated respiratory infection, Empirin Compound with Codeine provides an antitussive bonus in addition to relief of pain and bodily discomfort.

 **prescribing convenience:**
up to 5 refills in 6 months,
at your discretion (unless
restricted by state law); by
telephone order in many states.

Empirin Compound with
Codeine **No. 3**, codeine
phosphate* 32.4 mg. (gr. ½);
No. 4, codeine phosphate*
64.8 mg. (gr. 1) *Warning—may
be habit-forming. Each tablet
also contains: aspirin gr. ¾,
phenacetin gr. 2½, caffeine
gr. ½.



Burroughs Wellcome Co.
Research Triangle Park
North Carolina 27709



HERE

Respiratory tract

EMPIRIN[®] COMPOUND c CODEINE

#3, codeine phosphate* (32.4 mg.) gr. ½
#4, codeine phosphate* (64.8 mg.) gr. 1



Banana-Flavored Donnagel® PG

The civilized solution to the age-old problem of diarrhea.

The evolution of Donnagel® PG:

Kaolin and pectin to provide demulcent-detoxinant effects.

Belladonna alkaloids for antispasmodic benefits.

Powdered opium, the therapeutic equivalent of paregoric—without the unpleasant taste—to promote the production of formed stools and lessen the urge.

And a delicious banana flavor good enough for the most discriminating tastes.

All together in the evolutionary discovery that's the best-tasting way yet to treat acute, non-specific diarrheas.

Donnagel® PG

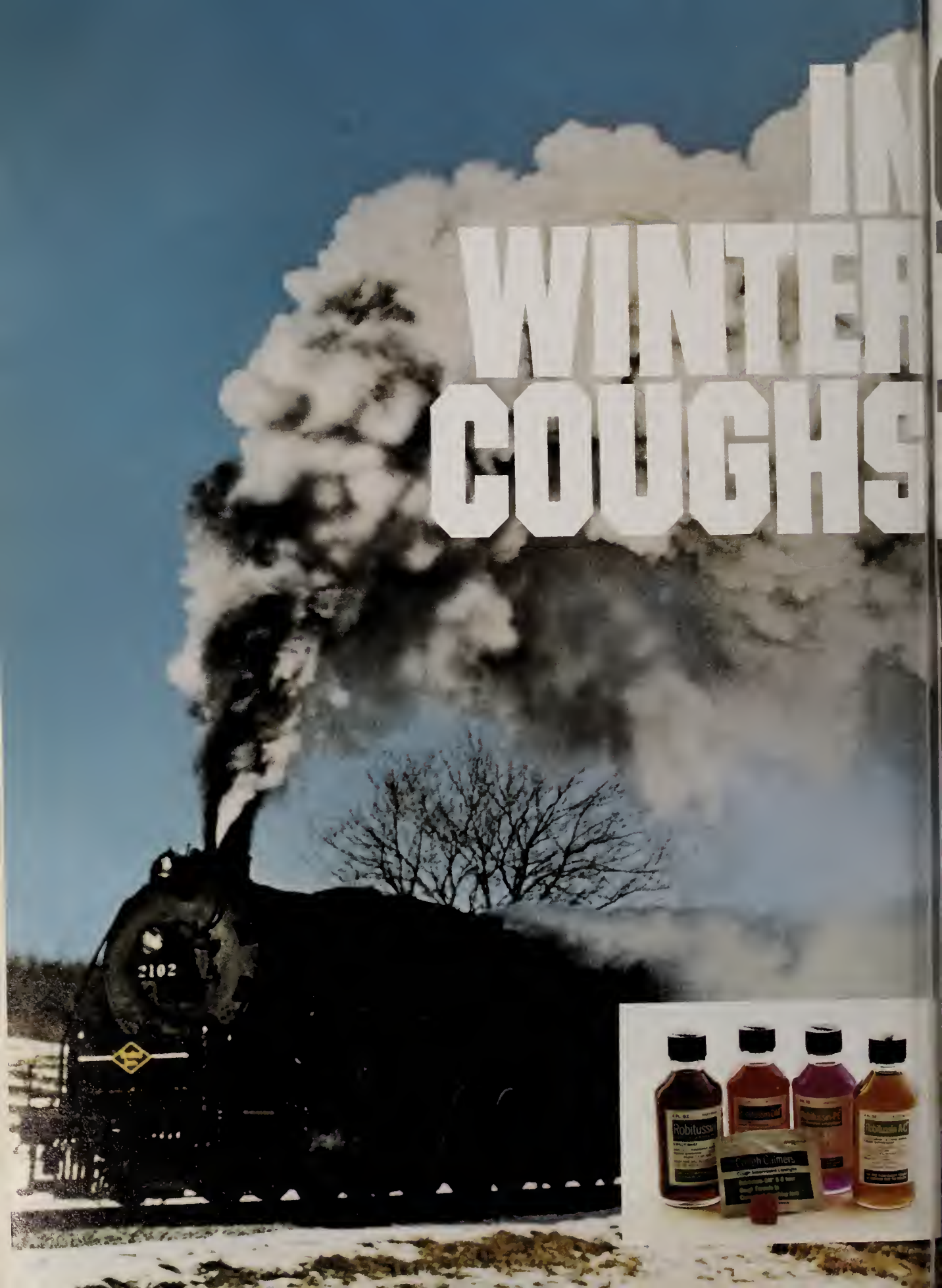
Donnagel with paregoric equivalent.
Each 30cc. contains:

Kaolin	6.0 g.
Pectin	142.8 mg.
Hyoscyamine sulfate	0.1037 mg.
Atropine sulfate	0.0194 mg.
Hyoscine hydrobromide	0.0065 mg.
Powdered opium, USP.	24.0 mg.
(equivalent to paregoric 6 ml.)	
(warning: may be habit forming)	
Sodium benzoate	
(preservative).	60.0 mg.
Alcohol, 5%	

Available on oral prescription or without prescription in compliance with applicable state and local law.

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ROBITUSSIN[®]

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Non-narcotic for 6-8 hr. cough control

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That Treats Your Patient's
Individual Coughing
Needs:

	Expectorant-Demulcent	Cough Suppressant	Antihistamine	Long-Acting (6-8 hours)	Nasal Sinus Decongestant	Non-Narcotic
ROBITUSSIN [®]	●					●
ROBITUSSIN A-C [®]	●	●	●			
ROBITUSSIN-DM [®]	●	●		●		●
ROBITUSSIN-PE [®]	●				●	●
COUGH CALMERS [®]	■	■		■		■

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A·H·ROBIN[®]

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The Weight of Professional Opinion

It's time for action to defend the laws and regulations that protect your patients against drug substitution.

**These professional and trade organizations are united
in supporting antisubstitution statutes and regulations:**

The American Academy of Dermatology

The Board of Directors of the
American Academy of Family
Physicians

The Executive Board of the
American Academy of Neurology

The Committee on Drugs of the
American Academy of Pediatrics

The American College of Allergists

The Executive Committee of the
American College of Obstetricians
and Gynecologists

The Board of Regents of the
American College of Physicians

The Board of Trustees of the
American Dental Association

The Board of Trustees of the
American Medical Association

The American Psychiatric Association

The Executive Committee of the
National Association of Retail
Druggists

The Board of Directors of the
Pharmaceutical Manufacturers
Association

The National Wholesale Druggists'
Association



Joint Statement on Antisubstitution Laws and Regulations

The purpose of this statement is to affirm the support of the participating organizations for the laws, regulations and professional traditions which prohibit the unauthorized substitution of drug products.

Traditionally, physicians, dentists and pharmacists have worked cooperatively to serve the best interests of patients. Productive cooperation has been achieved through mutual respect as well as a common concern for the ideals of public service. This mutual respect has been reflected, in part, by joint support over the years for the adoption and enforcement of laws and regulations specifically prohibiting unauthorized substitution and encouraging joint discussion and selection of the source of supply of drug products. The basic principles of medical, dental and pharmacy practice are thus utilized and preserved in the interest of patient welfare.

The antisubstitution laws have not obstructed enhancement of the professional status of pharmacy any more than they have in and of themselves guaranteed absolute protection from unsafe drugs, or freed physicians, dentists and pharmacists from their responsibilities to patients. As a practical matter, however, such laws and regulations encourage inter-professional communications regarding drug product selection and assure each profession the opportunity to exercise fully its expertise in drug usage, to the advantage of patients.

Physicians and dentists should be urged to increase the frequency and regularity of their contacts with pharmacists in selection of quality drug products, recognizing that

economies to patients can be improved through such communication, taking into account the patients' needs. The pharmacist's knowledge of the chemical characteristics of drugs, their mode of action, toxic properties and other characteristics that assist in making drug selection decisions should be utilized to the fullest extent practicable by physicians and dentists in serving their patients.

Since drug product selection entails knowledge derived from clinical experience, the physician's and dentist's roles in product selection remain primary and do not permit delegation of decisions requiring medical and dental judgments. A broader role in therapy will evolve for pharmacists as improved understanding and cooperation among the professions continue to grow.

There has been no evidence that there are convincing reasons to modify or repeal existing laws and regulations prohibiting the unauthorized substitution of another drug product for the one specified by a prescriber. It is our belief that such laws and regulations merit the joint support of the medical, dental and pharmaceutical professions and the pharmaceutical industry.

Add your opinion to the weight of other professionals and send it to your state assemblyman or legislator.

*Pharmaceutical Manufacturers Association
1155 Fifteenth Street, N.W., Washington, D. C. 20005*



Synthroid[®]

(sodium levothyroxine)



Supplied: **Tablets:** 0.025 mg., 0.05 mg., 0.1 mg., 0.15 mg., 0.2 mg., 0.3 mg., 0.5 mg., scored and color-coded in bottles of 100, 500, and 1000.

Injection: 500 mcg. lyophilized active ingredient and 10 mg. of Mannitol, U.S.P., in 10 ml. single-dose vial, with 5 ml. vial of Sodium Chloride Injection, U.S.P., as a diluent.

Synthroid-T₄



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PRESCRIBING INFORMATION

Antiminth (pyrantel pamoate) Oral Suspension

Actions. Antiminth (pyrantel pamoate) has demonstrated anthelmintic activity against *Enterobius vermicularis* (pinworm) and *Ascaris lumbricoides* (roundworm). The anthelmintic action is probably due to the neuromuscular blocking property of the drug.

Antiminth is partially absorbed after an oral dose. Plasma levels of unchanged drug are low. Peak levels (0.05-0.13 µg/ml.) are reached in 1-3 hours. Quantities greater than 50% of administered drug are excreted in feces as the unchanged form, whereas only 7% or less of the dose is found in urine as the unchanged form of the drug and its metabolites.

Indications. For the treatment of ascariasis (roundworm infection) and enterobiasis (pinworm infection).

Warnings. *Usage in Pregnancy:* Reproduction studies have been performed in animals and there was no evidence of propensity for harm to the fetus. The relevance to the human is not known.

There is no experience in pregnant women who have received this drug.

Precautions. Minor transient elevations of SGOT have occurred in a small percentage of patients. Therefore, this drug should be used with caution in patients with pre-existing liver dysfunction.

Adverse Reactions. The most frequently encountered adverse reactions are related to the gastrointestinal system.

Gastrointestinal and hepatic reactions: anorexia, nausea, vomiting, gastralgia, abdominal cramps, diarrhea and tenesmus, transient elevation of SGOT.

CNS reactions: headache, dizziness, drowsiness, and insomnia. Skin reactions: rashes.

Dosage and Administration. *Children and Adults:* Antiminth Oral Suspension (50 mg. of pyrantel base/ml.) should be administered in a single dose of 11 mg. of pyrantel base per kg. of body weight (or 5 mg./lb.); maximum total dose 1 gram. This corresponds to a simplified dosage regimen of 1 cc. of Antiminth per 10 lb. of body weight. (One teaspoonful = 5 cc.)

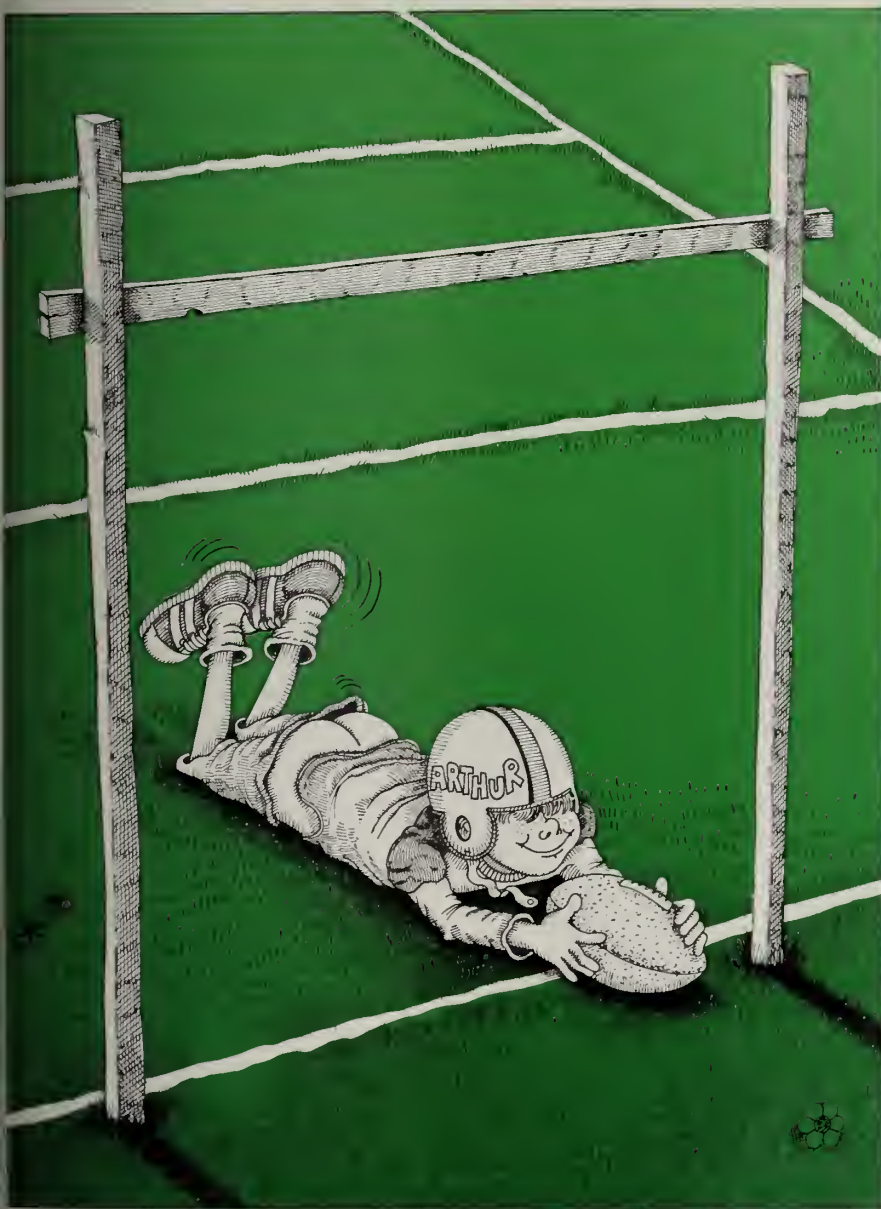
Antiminth (pyrantel pamoate) Oral Suspension may be administered without regard to ingestion of food or time of day; and purging is not necessary prior to, during, or after therapy. It may be taken with milk or fruit juices. Because of limited data on repeated doses, no recommendations can be made.

How Supplied. Antiminth is available as a pleasant tasting caramel-flavored suspension which contains the equivalent of 50 mg. pyrantel base per ml., supplied in 60 cc. bottles.

ROERIG 

A division of Pfizer Pharmaceuticals
New York, New York 10017

WORMS BLITZED



A single dose of Antiminth (1 cc. per 10 lbs. of body weight, 1 tsp./50 lbs. — maximum dose, 4 tsp.=20 cc.) offers highly effective control of *both* pinworms and roundworms.

Antiminth has been shown to be extremely well tolerated by children and adults alike in clinical studies.* Pleasantly caramel-flavored, it is non-staining to teeth and oral mucosa on ingestion... doesn't stain stools, linen or clothing.

One prescription can economically treat the entire family.

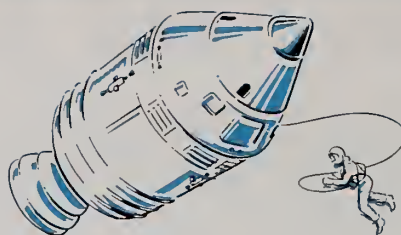
ROERIG *Pfizer*

A division of Pfizer Pharmaceuticals
New York, New York 10017

**Pinworms, roundworms controlled
with a single, non-staining dose of
ANTIMINTH[®]
(pyrantel pamoate)**

equivalent to 50 mg. pyrantel/ml.

ORAL SUSPENSION



Man in space, now fait accompli, re-emphasizes the importance of Uro-Phosphate therapy. Research into the effect of space travel on the astronaut reveals that weightlessness causes loss of bone calcium. As the bones are required to bear less and less of the weight of the body they lose calcium, increasing the calcium content of the urine. When physical activity is reduced, the acidity of the urine should be adjusted to keep increased calcium in solution . . . a prophylaxis to prevent kidney or bladder calculi.

Uro-Phosphate®

NOW A SUGAR-COATED TABLET

Each tablet contains: METHENAMINE, 300 mg.; SODIUM ACID PHOSPHATE, 500 mg.

Uro-Phosphate gives comfort and protection when inactivity causes discomfort in the urinary function. It keeps calcium in solution, preventing calculi; it maintains clear, acid, sterile urine; it encourages

complete voiding and lessens frequency when residual urine is present.

Uro-Phosphate contains sodium acid phosphate, a natural urinary acidifier. This component is fortified with methenamine which is inert until it reaches the acid urinary bladder. In this environment it releases a mild antiseptic keeping the urine sterile.

Uro-Phosphate is safe for continuous use. There are no contra-indications other than acidosis. It can be given in sufficient amount to keep the urine clear, acid and sterile. A heavy sugar coating protects its potency.

Dosage:

For protection of the inactive patient 1 or 2 tablets every 4 to 6 hours is usually sufficient to keep the urine clear, acid and sterile.

2 tablets on retiring will keep residual urine acid and sterile, contributing to comfort and rest.

A clinical supply will be sent to physicians and hospitals on request.



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POST GRADUATE EDUCATION

ADULT RESPIRATORY DISTRESS SYNDROME

Hall G. Canter, M.D.

Any disorder which involves 150,000 Americans a year results in 40-50% mortality and costs \$5,000 per patient demands attention. Such a disorder is the Adult Respiratory Distress Syndrome which results from a variety of direct and indirect pulmonary injuries. A common feature appears to be a leaky alveolar-capillary membrane which allows exudation of fluid into the lung interstitium and ultimately into the alveolar spaces. This results in a stiff lung and loss of surfactant activity causing impaired gas exchange.

The syndrome may occur following thoracic or extrathoracic trauma, such as major abdominal surgery. Shock, Septicemia, fat emboli and cardiopulmonary by-pass are frequent predisposing factors. Aspiration and viral pneumonia may lead to ARDS but usually not bacterial pneumonia. Peritonitis, pancreatitis, extensive burns, smoke or gas inhalation and drug overdose (heroin, methadone) have been reported as causal factors. The subjects previously have normal lungs and do not have left ventricular failure (cardiogenic pulmonary edema).

The syndrome presents as sudden dyspnea, tachypnea, cyanosis and refractory hypoxemia in a patient with one or more of the predisposing factors. The chest roentgenogram initially may be normal but soon develops the pattern of diffuse alveolar infiltrates with air bronchograms (non-cardiogenic pulmonary edema). With loss of surfactant and displacement of air from acinii a severe ventilation/perfusion imbalance develops. This causes hypoxemia which is refractory to oxygen-enriched mixtures because of increased venous admixture. Initially carbon dioxide retention does not occur as the patients hyperventilate sufficiently to maintain a normal or even low pCO_2 . However, as the syndrome worsens CO_2 retention may develop along with respiratory acidosis.

The altered physiology is caused by two major abnormalities—closure of air spaces and excessive pulmonary extravascular water. These lead to a decrease in lung compliance (stiff lung) and the marked ventilation/perfusion imbalance. The ultimate outcome depends not only on the degree and nature of the original injury but also on the prevention of further pulmonary injury.

Mainstays of therapy include measures to prevent alveolar collapse such as volume-controlled respirator with positive end-expiratory pressure if necessary and oxygen supplementation. In order to prevent oxygen toxicity one tries to avoid oxygen-enriched mixtures greater than 50%, but this is not always possible. Restricting fluids to 20-25 ml/Kg/24 hours and using potent diuretics one hopes to prevent further extravascular water accumulation. There is some evidence that heparin may help in the face of fat emboli or intravascular coagulation. Corticosteroids may be useful also by inhibiting leukocyte and platelet adherence as well as stabilizing lysosomes and enhancing surfactant secretion. Narrow-spectrum antibiotics based on appropriate studies may be life-saving.

Although the pathways leading to ARDS are multiple and the mechanism of lung injury not always known (ischemia, toxic, lysosomal release, etc.) the treatment plan is the same and is aimed at preventing alveolar collapse, maintaining oxygenation and avoiding further lung injury from fluid overload, infection and oxygen toxicity.

Dr. Carter is Associate Professor of Medicine, and Chief, Pulmonary Disease Section, Pulmonary Division at Georgetown University Medical Center.

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Since 1905, Peoples has filled over 145 million prescriptions. *The next one we fill is just as important to us as all those in between.*



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Sugar-free medication for the obese patient.



For the patient who requires maximum palatability.

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effective ways to promote
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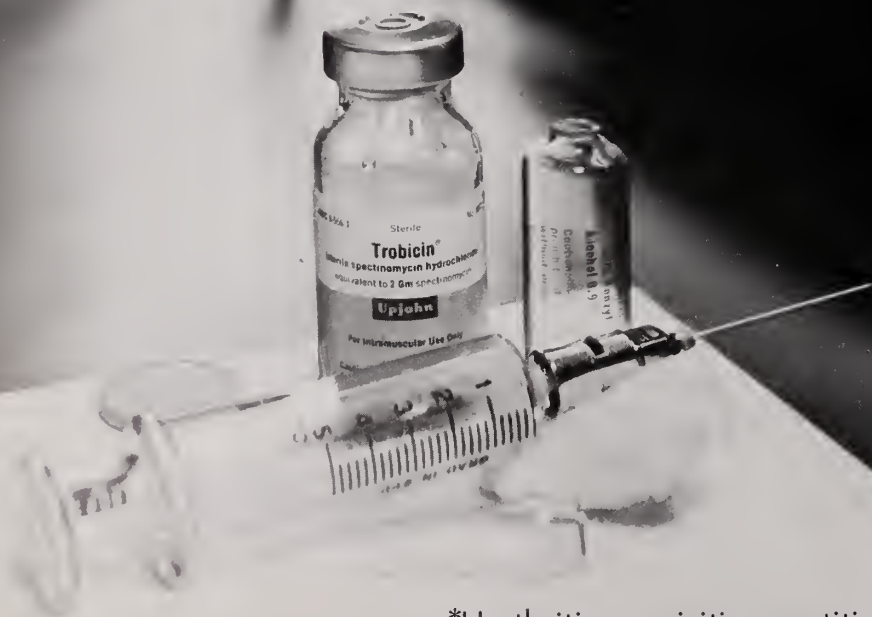
in the treatment of constipation or diarrhea

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acute gonorrhea

This patient
just received
an effective, private,
physician-controlled
treatment.

It took just one short visit



*Urethritis, cervicitis, proctitis when due
to susceptible strains of *N. gonorrhoeae*

Trobicin—The advantage of injectable therapy.

Once Trobicin is injected, treatment is usually complete; there can be no problems with patients sharing, skimping, skipping or forgetting medication.

Trobicin—The aspect of privacy.

There are no prescriptions to fill, no capsules to take. Neither family, friends nor co-workers need know or suspect the patient's problem.

Trobicin—Indication and dosage.

Spectinomycin is indicated only for use in acute urethritis and proctitis in the male and acute cervicitis and/or proctitis in the female when due to susceptible strains of *N. gonorrhoeae*. The usual dosage for Trobicin in adult males is 2 grams intramuscularly[†]; 4 grams intramuscularly in females.

Trobicin—Not effective for syphilis.

Trobicin is not effective for any stage of syphilis. Trobicin may mask or delay the symptoms of incubating syphilis. If concurrent syphilis is suspected, follow the patient serologically for at least 3 months. Patients with syphilis should receive adequate specific anti-syphilitic therapy with an appropriate antibiotic. Trobicin is contraindicated in patients previously found hypersensitive to it.

Intramuscular

...and **Trobicin**[®] 2 gm and 4 gm vials sterile spectinomycin hydrochloride

Sterile Trobicin

Sterile Trobicin (spectinomycin hydrochloride)
For Intramuscular Injection:

2 gm vials containing 5 ml when reconstituted with diluent.

4 gm vials containing 10 ml when reconstituted with diluent.

an aminocyclitol antibiotic active *in vitro* against most strains of *Neisseria gonorrhoeae* (MIC 7.5 to 20 mcg/ml). Definitive *in vitro* studies have shown no cross resistance of *N. gonorrhoeae* between spectinomycin and penicillin.

Indications: Acute gonorrheal urethritis and proctitis in the male and acute gonorrheal cervicitis and proctitis in the female when due to susceptible strains of *N. gonorrhoeae*.

Contraindications: Contraindicated in patients previously found hypersensitive to spectinomycin.

Warnings: Not indicated for the treatment of syphilis. Antibiotics used to treat gonorrhea may mask or delay the symptoms of incubating syphilis. Patients should be carefully examined and monthly serological follow-up for at least 3 months should be instituted if the diagnosis of

syphilis is suspected.

Safety for use in infants, children and pregnant women has not been established.

Precautions: The usual precautions should be observed with atopic individuals. Clinical effectiveness should be monitored to detect evidence of development of resistance by *N. gonorrhoeae*.

Adverse reactions: The following reactions were observed during the single-dose clinical trials: soreness at the injection site, urticaria, dizziness, nausea, chills, fever and insomnia. During multiple-dose subchronic tolerance studies in normal human volunteers, the following were noted: a decrease in hemoglobin, hematocrit and creatinine clearance; elevation of alkaline phosphatase, BUN and SGPT. In single- and multiple-dose studies in normal volunteers, a reduction in urine output was noted. Extensive renal function studies demonstrated no consistent changes indicative of renal toxicity.

Dosage and administration: Keep at 25° C and use within 24 hours after reconstitution with diluent.

Male—Inject 5 ml intramuscularly for a 2 gram dose. Patients with gonorrheal proctitis and patients being re-treated after failure of previous antibiotic therapy should receive 4 grams (10 ml). In geographic areas where antibiotic resistance is known to be prevalent, initial treatment with 4 grams (10 ml) intramuscularly is preferred.

Female—Inject 10 ml intramuscularly for a 4 gram dose.

How supplied: Vials, 2 and 4 grams—with ampoule of Bacteriostatic Water for Injection with Benzyl Alcohol 0.9% w/v. Reconstitution yields 5 and 10 ml respectively with a concentration of 400 mg spectinomycin per ml (as the hydrochloride). For intramuscular use only. **Susceptibility Powder**—for testing *in vitro* susceptibility of *N. gonorrhoeae*.

Caution: Federal law prohibits dispensing without prescription.

For additional product information see your Upjohn representative or consult the package insert.

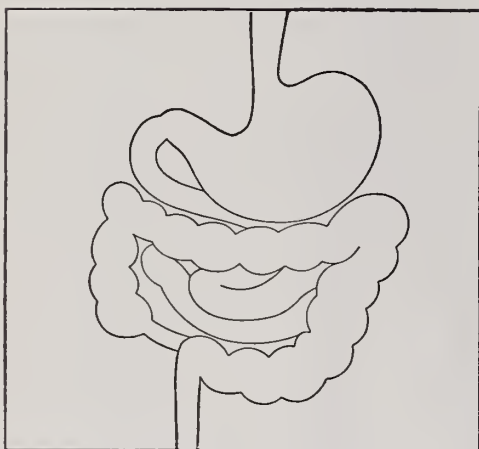
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MED B-5-S (MBR-1)

For patients with gonorrheal proctitis and for patients in geographic areas where antibiotic resistance is known to be prevalent, initial treatment with 4 grams is preferred.

in “Gasspastic” conditions



The GI tract in spasm is commonly a “gas trap.”

Sidonna® is formulated to release entrapped gas, as well as to provide antispasmodic/sedative effects.

In addition to the traditional combination of belladonna alkaloids and butabarbital (warning: may be habit forming.), Sidonna contains simethicone—a non-systemic defoaming agent that “lyses” gas bubbles on contact.

Sidonna has the ability to relieve GI spasm, pain **and gas** in the irritable bowel syndrome, spastic colon, pylorospasm, gastroenteritis, gastritis, nausea, nervous indigestion, or gastric and duodenal ulcer.

Sidonna can calm GI spasm...control anxiety...and release entrapped GI gas from the system.

Sidonna can do more for your “gasspastic” patient. Try him on 1 or 2 tablets before meals and at bedtime.

Sidonna®

Each scored tablet contains: Specially activated simethicone 25 mg.; hyoscyamine sulfate 0.1037 mg., atropine sulfate 0.0194 mg., hyoscine hydrobromide 0.0065 mg. (equivalent to belladonna alkaloids [as bases] 0.1049 mg.) and butabarbital sodium N.F. 16 mg. (Warning: May be habit forming.)

can do more

Contraindications: Anticholinergics should not be used in patients with glaucoma, known prostatic hypertrophy, or pyloric obstruction. Urinary retention may indicate the presence of prostatic hypertrophy. If it occurs, the dose should be reduced or the drug withdrawn. Also contraindicated in patients with known hypersensitivity to one of the components.

Side Effects: Dryness of the mouth, blurred vision, dysuria, skin rash, constipation or drowsiness may occur.

Reed & Carnrick / Kenilworth, New Jersey 07033

BOOK REVIEWS

Gastroesophageal Reflux in Hiatal Hernia. DAVID B. SKINNER, M.D., RONALD H. R. BELSEY, M.S., F.R.C.S., THOMAS R. HENDRIX, M.D. AND GEORGE D. ZUIDEMA, M.D. Price, \$12.95. Pp. 224 with illustrations. Boston, Massachusetts: Little Brown & Company, 1972.

This monograph, edited by three surgeons and a gastroenterologist, seeking contributions from radiologists and pathologists, summarizes much of the available information concerning the entities of gastroesophageal reflux and hiatal hernia. There is much that is good in this text to recommend it, but the reader must be exceedingly discriminating so as not to be persuaded by those inaccuracies which occur. The text is divided into 15 chapters covering anatomy, physiology, pathology, clinical manifestations, diagnostic considerations, and finally several chapters devoted to medical and surgical management of this problem. Overall one would have to say that the content of the several chapters varies greatly. Contradictions in one section from statements previously made in another abound.

Perhaps the single biggest objection I have is the inclusion of hiatal hernia in the title. Although the authors, and particularly Dr. Hendrix in his chapter on pathogenesis of esophageal reflux, recognize that a hiatal hernia need not be a pre-condition for such reflux and that it occurs as commonly in the absence of a hiatal hernia as in the presence of hiatal hernia, and that in magnitude of lower esophageal sphincter pressure appears to be the critical determinant of the occurrence of reflux, nonetheless, the inclusion of hiatal hernia in the title and its subsequent reiteration time and again by all authors during the text, suggest a certain primacy of this phenomenon in the pathogenesis of reflux. Whereas this in fact may be true, available medical evidence suggests that it is not true. Strengths of the book are the sections on function of the gastroesophageal segment by Hendrix, to a lesser degree that on symptoms by Skinner, and in particular the pathology of reflux esophagitis by Yardley in which consideration is given to surgical as well as biopsy specimens. Radiologic examination chapter is also most useful, however, it lacks reference to some important references particularly controversies about lower esophageal (Schatzki's ring) and perhaps emphasizes too much the detection of a hiatal hernia.

The chapter on diagnostic tests is most helpful in pointing out that the reliability of tests from the standpoint of occurrences of false-positives and false-negatives, however several of the tests recommended are not critically assessed. For

instance, in describing the pH reflux test, Skinner suggests prior infusion of 300 units of 0.1 N HCl facilitates the detection of reflux by a pH probe in the gullet. Based on recent observations, many of which were published prior to this text, one might predict that a fall in intragastric pH by such acid infusion would exert a negative feed back on gastrin release, and, hence, result in a fall of lower esophageal sphincter pressure tending to enhance reflux. So that the very basis of the test, which was emphasized as an effective diagnostic tool, is suspect. The chapter on esophagoscopy I found useless, imparting no valuable information.

My overall impression is that there is much of usefulness to the specialist who is clearly able to discern the controversial and inaccurate statements. That such occurs is in part due to the rapidly expanding information in this particular area after a number of years of inactive investigation. I cannot comfortably recommend this book for general use. STUART H. DANOVITCH, M.D.

Aging and Mental Health. ROBERT N. BUTLER, M.D. AND MYRNA I. LEWIS. Price, 5.95 Pp. 289 with illustrations. St. Louis: The C. V. Mosby Company, 1973.

The authors stress a positive psychosocial approach in considering this subject. They discuss and take a general view of aging, including emotional problems, physical disorders (both functional and organic) and a wide range of related subjects such as racism, sexism, retirement, crime (with attention directed towards the elderly as victims), alcoholism and sexuality, interfamilial relationships and therapy ranging from evaluation, socioeconomic factors and medical treatment. Home care and nursing, institutional care and special treatment of those conditions involving insomnia, organic brain syndrome, retirement syndrome, Parkinsonism, stroke, hearing and visual impairment and malnutrition are skillfully expounded.

Research is often aimed at prolonging life and improving physical ailments, ie. arteriosclerosis and senility, arthritis and osteoporosis and other degenerative diseases rather than making life more satisfying and dignified. It could also increase the period of productive life and shorten the period of senescence.

BOOK REVIEWS

Emphasis is placed on the continued involvement in life not only by the older person but also a recognition of this by society so that the individual continues to have an opportunity for a systematic meaningful existence. Society has a prejudice against such people because they are old which the authors call ageism. This is more noticeable regarding the female. They point out that this very group has much to offer and might well be part of the immense liberation movement which is enjoying a striking increase in popularity at this time.

Old age is a multiple determined experience that depends on the balance of physical and intricate social forces.

A myriad of services closely affect the mental health of old people—welfare agencies, food stamp programs, social security and Medicare, health insurance companies, churches, public transportation, police protection and pharmacists. The absence, presence and style of functioning of any of these can influence emotional well being or cause stress.

The book contains much statistical data and examples follow in the United States: 20 million people are 65 years or older of whom 10 million people are 73 years and 106,000 people are over 100 years of age. The number of white females (75+ years) are 156.2 per 100 males, whereas, the number of black females (1970 census) are 131 per 100 males. Life expectancy of white men is 67.5 years while the life expectancy of black men is 60.1 years (to the reviewers this was a surprise as it was believed that life expectancy was longer). Most elderly men are married while most elderly women are widows.

The authors recognize also problems of other minority groups as Mexican-Americans (Chicanos), American Indians and East Asian-Americans, ie. Japanese, Chinese and Filipinos. Because of differences in cultural aspects of these groups and due to circumstances through governmental policies in the past, their problems and the care of the elderly have been divergent in its individual, socioeconomic and familial context.

This book, from which quotations have been incorporated, is recommended reading with special value to social workers and is of interest to general practitioners lest they forget those other attributes and forces concerning the elderly, aside from the physical deteriorating diseases and mental states and/or problems.

JOHN STUBENBORD, M.D.

Labor-Management Relations in the Health Services Industry. NORMAN METZGER AND DENNIS D. POINTER. Price, \$17.50. Pp. 360. Washington, D.C.: Science and Health Publications, Inc., 1972.

This is an excellent book for hospital administrators. However, it is also a useful and interesting book for physicians, particularly those interested in hospital functions. It details the increasing role and status of the hospital in the health care industry. Of particular note is that the statements and conclusions made by the authors are supported by facts and figures in tables and footnotes from established authorities and publications in the field. In addition, there are numerous quotes and references from distinguished sources.

The book starts with a short history of hospitals detailing their growth to their present status in the health delivery system. For a more complete understanding there is a classification of hospitals coupled with an explanation of the nature of the hospital labor force. The authors detail the growth of the labor force, tracing the origin and growth of hospital unions with explanations for this phenomenon.

The book then gives an overview of collective organization activity in hospitals from their inception early in this century until the present. In the course of this chronology, the authors give an insight into the role of hospitals in recognizing the unions and their responsibility in getting them established.

In order to explain federal legislation regarding labor laws as they affect hospitals and hospital unions, the authors give an overview of labor legislation in general. In particular, the book explains the status of hospital unions under these federal laws. The status of unions under labor laws is completed by any overall analysis of state laws. This overview shows great variation among the states, ranging from no laws to what might be considered very strong pro-union legislation. Some states have laws which allow employees to continue their employment without union affiliation—so-called open shops or right to work laws.

For those familiar with the types of hospital employees, the authors present a picture of each type as a collective employee in the health care industry including their common interests and antagonisms. A good deal of the remainder of the book develops the unionism concept and role as it applies to the various types of employees—professional and nonprofessional.

The last chapters are devoted to detailing the inception and establishment of a union in a hospital. This is presented by the authors from the point of view of the employees, the union, the hospital, and the public. The book then details the process of union recognition. That accomplished there is an exposition of the necessary preparation to negotiate a basic collective bargaining agreement. The authors detail in particular the negotiation of wages, health and pension plans. The health care industry, in general, and voluntary hospitals, in particular, form a unique situation in the collective bargaining process. The possibility of harm to patients and the nature of hospital reimbursement are the most important of a number of elements and factors which particularize hospital and union relationships. The reader is furnished with an explanation and understanding of the various mechanisms, while at the same time exposing the virtues and defects of these processes. It is presented in the form of advice to the participants.

The book concludes with a narration of events which the authors denote as living with the negotiated agreements and finally a complete review of "strikes."

I believe the book is a useful contribution to the literature on labor-management relations in the health services industry. It gives both theory and practice. I recommend to those directly, and even indirectly, interested in this field.

HAROLD L. HIRSH, M.D.

Medical Education in the United States Before the Civil War. WILLIAM FREDERICK NORWOOD.

Price, \$21.00. Pp. 487. New York: Arno Press and The New York Times, 1972.

Very interesting book which surveys the development progress of the United States system of medical instruction and medical institutions of learning up to the time of the Civil War. The author concentrates his efforts on presenting information on many relatively unknown institutions of medical learning that existed in the United States prior to the Civil War. He does not neglect the larger better

known schools, but presents in an interesting fashion background information on a number of medical schools which no longer exist, yet played a noticeable role in the formulation of and progress of medical education in America. His comments are presented in an interesting, readable fashion. They examine a phase of American medical history which, until recent years, has not been extensively discussed by medical historians. The sections dealing with the medical schools of Virginia, Maryland, Pennsylvania and the District of Columbia were of particular interest. There are concise chapters on methods of instruction, curricula, medical training costs and financial support as well as the individual schools that flourished and floundered during the period covered by this publication. It is interesting to note that the trials and tribulations of medical school faculties and administrations in obtaining adequate financial support were quite similar to the problems faced by these groups today. The problems of women in medicine existed even in the days prior to the Civil War. As schools were established and the domain of the traditional female midwife was invaded by thousands of trained male accoucheurs, the female practitioners were driven from the field. To counteract these trends the women crusaders, Caroline H. Dall, Olive Schreiner and Catherine Beecher were active in the development of the Boston Female Medical School which came into being in 1848 as the first female medical school in the United States. It began on November 1, 1848 with a class of twelve pupils. On March 11, 1850, the Women's Medical College of Pennsylvania officially came into being followed shortly by the Women's Medical College of New York Infirmary and New York Medical College and Hospital for Women, so that prior to the Civil War four independent medical schools for women were in existence. A total of ninety-one medical schools and colleges are discussed in this book. To those interested in medical history and in the background of medical education in the United States prior to the Civil War, this is an interesting, readable publication, well prepared and researched, which is worthy of your leisure reading time.

BRUCE I. SHNIDER, M.D.

What's on your patient's face...

may be more important than his chief complaint

Patient P.T.* seen on 3/29/67 shows typical lesions of moderately severe keratoses. Note residual scarring on ridge of nose from previous cryosurgical and electrosurgical procedures.



Patient P.T.* seen on 6/12/67, seven weeks after discontinuation of 5% FU cream. Reaction has subsided. Residual scarring not seen except that due to prior surgery. Inflammation has cleared and face is clear of keratotic lesions.

*Data on file,
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165.

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INDEX TO ADVERTISERS

Insurance

Corroon & Black, Russel, Inc.	92
Mutual of Omaha	85
Ralph W. Lee & Company	105

Nurse Registries

Association of Undergraduate and Practical Nurse Registry	92
District of Columbia Manpower Administration	106

Nutrition Education

Dairy Council of Greater Metropolitan Washington, D.C.	2
--	---

Pharmaceuticals

A. H. Robins	81
Burroughs Wellcome & Company	78
Burton Parsons & Company	95

Flint Laboratories	84, 89-90
Eli Lilly & Company	8
McNeil Laboratories	4
Pharmaceutical Manufacturers Association	82-83
William P. Poythress & Company	88
Reed & Carnick	98
Roche Laboratories	102-103, c3, c4
J. B. Roerig	86-87
G. D. Searle & Company	76-77
Smith, Kline and French	75
The Upjohn Company	96

Pharmacy

Peoples Drug Stores	94
---------------------------	----

Sanitarium

Kalorama Convalescent Home Inc.	92
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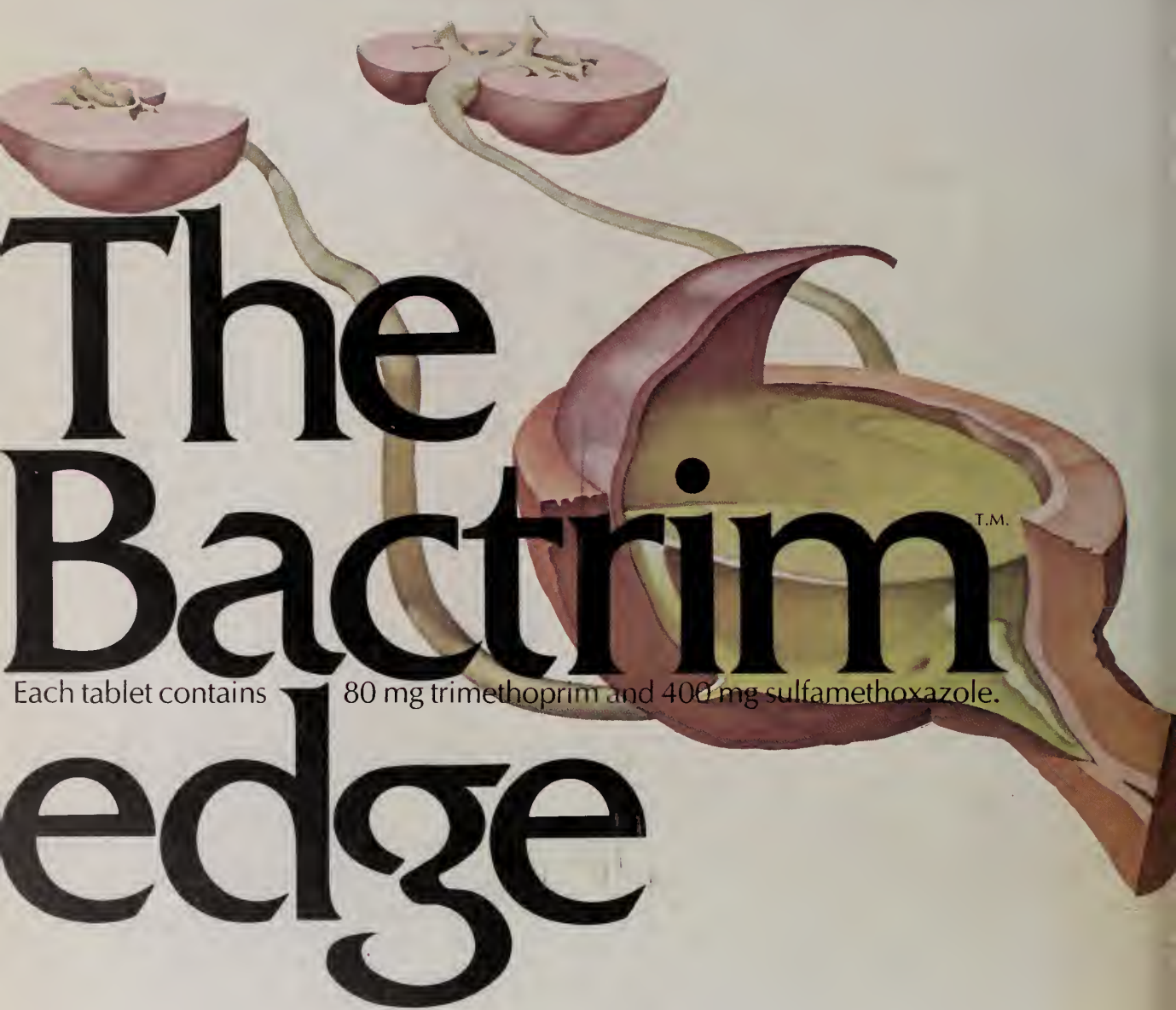
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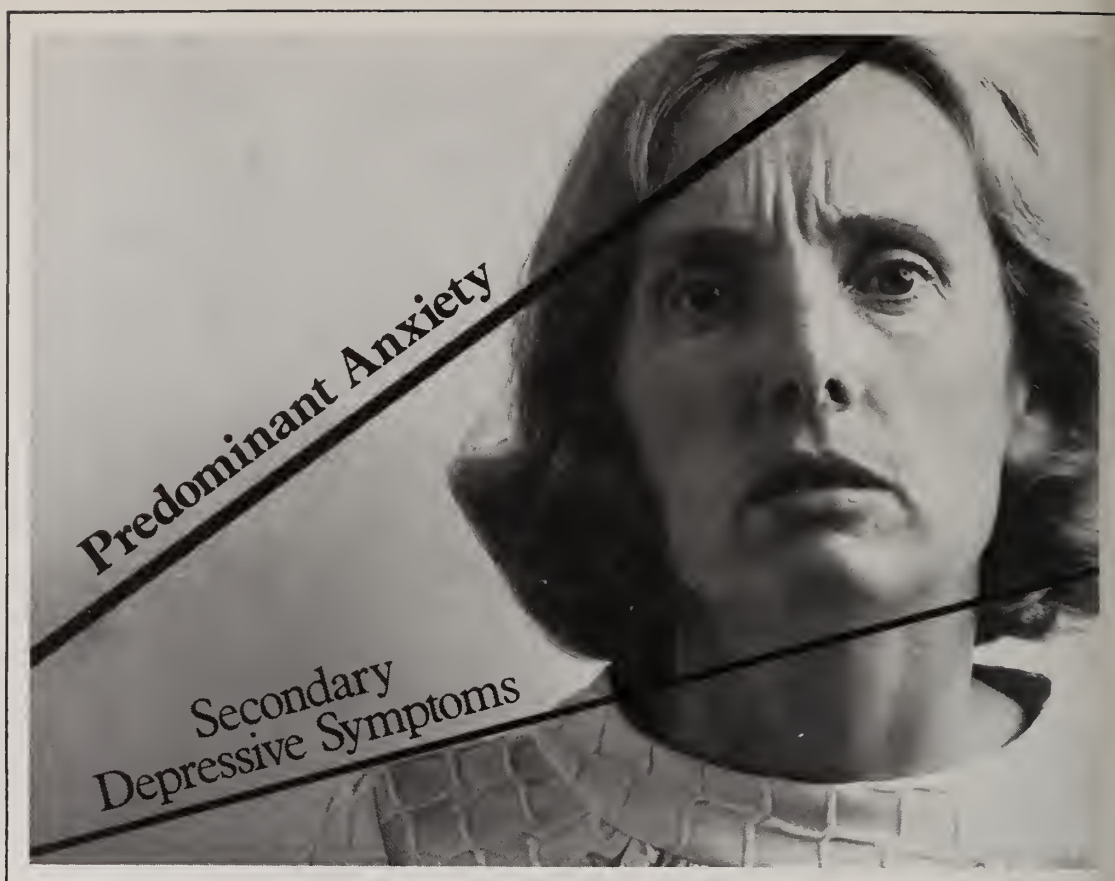
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Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant

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* Ex officio member of the Executive Board

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CONTENTS

SCIENTIFIC ARTICLES

- Pneumothorax During Respirator Therapy. Jack E. Zimmerman, M.D., Burdett S. Dunbar, M.D. and C. Herman Klingemaier, M.D. 107
- Response of Asthmatic Airways to Intravenous Bradykinin and Histamine. Harold H. Newball, M.D. 111
- Immunologic Studies in Nitrofurantoin Induced Pulmonary Disease. Robert A. Goldstein, M.D. and Bernard W. Janicki, M.D. . . 115
- Subjective Response to Therapy in Chronic Obstructive Lung Disease. Harold M. Silver, M.D. and Olga M. Eaton, M.D. 120
- Busulfan Lung Complicated by Pneumocystis carinii and Cytomegalovirus Infection. Gerald I. Green, M.D., Richard L. Levin, M.D., Lawrence E. Pierce, M.D. and Philip Witorsch, M.D. 124
- The Definitive Diagnosis and Treatment of Pulmonary Disease By Selective Bronchial Catheterization. S. David Rockoff, M.D. . 129

SPECIAL ARTICLE

- Recent Advances in Respiratory Therapy. Ronald J. Karpick, M.D. 137

OTHER FEATURES

- President's Message 5
- Small Pox Vaccination—Passing of an Era. Clifton R. Gruver, M.D.
- Editorial 6
- Pulmonary Medicine. Harold M. Silver, M.D.
- Scientific Editorial 7
- The Clinical Use of Heparin. Lawrence E. Pierce, M.D.
- Medical Society of D.C. Committee Listing for 1974 159
- Post Graduate Education 147
- Prudent Nutrition and the Pill. Joseph Giere, M.D.
- The View Box 110
- Edited by Gunther J. Augustin, M.D.
- ECG Problems 150
- Edited by Robert R. Montgomery, M.D.
- Book Reviews 169
- Genetic Control of Immune Responsiveness.
(McDevitt and Landy) Reviewed by Phillip Periman, M.D.
- The Drug Abuse Controversy. (Brown and Savage) Re-
viewed by Arthur Ruskin, M.D.
- Information for Authors 172
- Advertising and Subscription Information 174
- Index to Advertisers 174

PRESIDENT'S MESSAGE

Small Pox Vaccination—Passing of an Era

Whenever a health law that has been around since Civil War times is considered for repeal, such action warrants explanation and more than passing commentary. H.R. 8747 is a bill introduced to Congress to repeal Section 274 of the Revised Statutes of the United States relating to the District of Columbia. This law required compulsory Small Pox Vaccination for all public school students.

Universal small pox vaccination is flavored historically, initial efforts toward that goal having promulgated by no less than Thomas Jefferson and Oliver Wendell Holmes. It became a public health mandate in our city by an Act of Congress in 1864.

In the Archives of our own Medical Society of the District of Columbia (covering the period 1817-1909) there appear several references to Small Pox and vaccination. You will remember that our Society was first organized in 1813, and is the only state medical society to be chartered by the Congress of the United States. In 1828, the Society held extra meetings and discussed measures to arrest the spread of Small Pox. Reference is made to a meeting in January 19, 1846 which was held to allay excitement caused by the prevalence of Small Pox in the District of Columbia. Papers were read to the Society in 1864 and again in 1865 on the use of vaccination against Small Pox, and the Society adopted a resolution stating its views were in accord with those of the Committee of The American Medical Association on the value and necessity of universal vaccination. In 1868, a committee was appointed to consider the best means of introducing the vaccine virus into use, and preserving it for use by members of the Society. Our library indicates the Society further dealt with the presence of Small Pox in the community in 1872 and 1877. In 1894, another outbreak occurred and a committee again was appointed to convey to the public the importance of vaccination as prophylaxis. There is no further reference to Small Pox after that point in our Archives, but it is obvious that the development and universal use of Small Pox vaccine provided one of the major scientific contributions to world public health in the history of medicine.

Why, then, the move to repeal?

A major decline in the existence of the disease in the U.S. occurred in the 1930's. The last case to be introduced to the District of Columbia was in 1932. The last documented case in the entire U.S. was in 1949. The current probability of a case being imported into the U.S. is estimated at about once in every 18 years.

With our heretofore policy of mass immunization of preschool children, immunity levels of overall population nevertheless remained low—in other words, repeated vaccinations must be accomplished throughout life to maintain high levels of immunity. Surveys suggest less than 20% of our total population in the U.S. is fully protected.

The reduction of the chance of importation and effective control should it occur can be accomplished by continuing a program of *selective* vaccination directed toward international travelers to and from any endemic Small Pox area of the world, not permitting access to these shores without presentation of a valid certificate of vaccination; and to hospital and other health personnel who would in most instances be initial contacts with a victim and might in turn be innocently responsible for transmitting the disease further into the populace—Small Pox Vaccination is recommended every 3 years for this group.

Mandatory universal Small Pox vaccination is fraught with many complications—some serious, life-threatening, even death-dealing. Since 1970, all 50 states have abandoned the process. The District of Columbia is the only jurisdiction remaining with such a statute on the books. Risk of complications is probably the foremost reason for repealing the law.

In 1968 (the most recent survey), over 14 million people were vaccinated. Sixteen cases of encephalitis, 11 cases of Vaccinia Necrosum, 126 cases of eczema vaccinatum vaccination, and a substantial number of lesser complications (many still requiring hospitalization), for a total of 9 deaths and 500 serious complications were recorded in that one year alone. The majority of these occurred in primary vaccinees.

So it has come to pass that morbidity and mortality of the prophylaxis have reached proportions greater than the current presence of the disease warrants.

The policy of *selective* vaccination has been recommended by the Public Health Service Advisory Committee on Immunization Practices, and carries the endorsement of the American Medical Association, the American Academy of Pediatrics, the American Academy of Family Practice, and the Association of State and Territorial Health Officers.

The Committee on Communicable Disease of the Medical Society of the District of Columbia recommended this policy to its Executive Board in 1971, and re-affirmed its position in January, 1973.

On January 22, 1974, the House District Committee held hearings on H.R. 8747. Dr. Raymond Standard, Director of Public Health for the District of Columbia, testified in support of this bill, and requested also that Congress act expeditiously so as to prevent the necessity of vaccination of children about to enter school this fall, indicating that two hospitalizations have resulted in the past 6 months alone from complications of Small Pox Vaccination of children for purpose of school admission.

Representatives of your Medical Society made a presentation at that hearing to lend professional and community support to Dr. Standard's request. It is likely that 110 years of mandatory universal vaccination against Small Pox has come to an end. Close epidemiologic monitoring will be necessary to determine that it should remain so.



CLIFTON R. GRUVER, M.D.
PRESIDENT

Editorial

PULMONARY MEDICINE

This issue, devoted to pulmonary diseases, is a testimony to the expansion of horizons in pulmonary medicine. At first the domain of the tuberculosis specialist sequestered in a sanitarium; however it has become an essential component of patient care, be it in office or hospital. Pulmonary function, respiratory therapy, and pulmonary physiotherapy have been recognized as essential services. The questions are how best to organize and utilize them, rather than whether they are needed.

There are, however, three major areas where large gaps in current knowledge require continued effort. They include:

1. *Chronic obstructive pulmonary disease (COPD).*

This group of diseases is most important in terms of mortality, morbidity, and prevalence. While there have been major improvements in the management of acute respiratory failure, there are key areas of etiology, natural history, meaningful classification and evaluation of therapy which remain elusive. Etiological factors such as alpha one antitrypsin deficiency have opened the whole question of proteolytic systems in pathogenesis. The role of cigarette smoking is established, but cigarette consumption continues to rise, indicating that the medical profession has singularly little to offer in dealing with this behavioral and possibly pharmacological problem. Air pollution has been implicated in causing exacerbations and complications in COPD, but the exact elements are not completely understood and suggestions for patient protection during episodes range from gratuitous to puerile.

Treatment is a subject of continuous contention. What medications should be employed and what is the therapeutic dose for long term use? More important, does treatment make any difference in the ultimate rate of progression of the disease? Many studies show continued decline in function to be the rule, but there is always some five to ten percent of patients who remain stable or actually improve over the long haul. The realization that this is possible should encourage vigorous therapy, and at the same time should encourage attempts to elucidate the characteristics which determine prognosis. In so chronic a disease group, there is need to understand the patient attitudes toward himself and his disease, and to influence behavior so that treatment is indeed used, exercise therapy is practiced, and vocational and daily living activities are sustained or expanded.

2. *Pulmonary malignancy.* The best surgical, radiotherapeutic, and medical treatment is ineffective in more than ninety percent of patients. This is despite the fact that there is no shortage of skilled thoracic surgeons, superior anaesthesia, and informed pre- and post-operative medical management. While immunological or chemotherapeutic means may provide ultimate answers, at least earlier diagnosis and better staging are needed now. There is a clear need for the development of techniques for sputum cytology which are applicable to mass screening. Fibroptic bronchoscopy for examination of the smaller bronchi with lavage or brushing to determine the site of pre-radiographic malignancy may be of value. Biochemical tests to detect the products of malignant cells may be visionary, but could prove out. Right now, a more extensive study of staging, with bilateral scalene, mediastinoscopic, and carinal biopsies, and possibly liver and brain scans, should be explored more systematically so that those persons who cannot be cured by surgery may be spared it and receive the best chance for radiotherapy.

3. *Diseases of immune response.* We take for granted the contribution of allergists in the management of true bronchial asthma, but this is just the top of the iceberg in pulmonary immunology. Hypersensitivity pneumonitis in response to inhalation of substances ranging from pigeon droppings to thermophilic fungi has been identified, and commercial immunodiffusion kits are now available for diagnosis. Pulmonary reactions from medications provide an ever expanding list of possible methods for study. Immunosuppressants and steroids have brought forth a new frequency of previously rare diseases such as cytomegalic virus, pneumocystis, and tissue invasion by fungi which are not usually pathogenic. Diseases which are associated with altered immunity, such as lymphoma and leukemia, provide enigmas when pulmonary infiltrates develop. The need for less traumatic means of diagnosis for these fragile patients, for better anti-infective agents, and the development of better ways to manipulate immunological responsiveness present opportunities as yet unrealized.

In summary, pulmonary medicine has expanded to include problems as diverse as those reported in this issue. It may be expected that there will be further expansion, encouraged by the scientific curiosity of its practitioners and by the ability to listen, understand, and attempt to resolve the problems which our patients bring us daily.

HAROLD M. SILVER, M.D.

SCIENTIFIC Editorial

ANTICOAGULATION I: THE CLINICAL USE OF HEPARIN

Among mucopolysaccharides, heparin is unique in its ability to inhibit blood coagulability and induce release of lipoprotein lipase after injection into mammalian species. It was incidentally discovered in 1916 by Dr. Jay McLean during investigation of thromboplastin potential in tissue extracts from the brain and liver, hence the origin of the name, heparin.¹ Chemical purification by Dr. Charles Best in Canada led to its first human administration in 1935 and three years later it was introduced to the United States as treatment for thrombophlebitis affecting Dr. Irving Wright in New York City.

Indications For Use:

1. Deep venous thrombosis
2. Pulmonary embolism
3. As immediate preliminary anticoagulation prior to long-term oral administration of coumadins
4. Coagulation defects associated with intravascular coagulation
5. Extracorporeal circulation (hemodialysis, cardiac surgery etc.)
6. Acute peripheral arterial occlusion
7. Controversial areas:
 - post myocardial infarction^{2a, 2b, 3}
 - congestive heart failure undergoing diuresis
 - CNS transient ischemic attacks
 - management of severe burns⁴

Relative contraindications:

1. Active bleeding
2. Recent (<2 years) cerebral hemorrhage or SBE
3. Severe hypertension and/or known vascular aneurysm
4. Untreated polycythemia rubra vera
5. Idiopathic macroglobulinemia in some patients.

Side effects:

1. Acute hypersensitivity (very rare)⁵
2. Alopecia (rare)
3. Infrequent induction of platelet aggregation thrombocytopenia^{6a, 6b}
4. Aggravation of osteoporosis with long-term usage (>1 year)⁷
5. Delayed collagen synthesis (wound healing) during first week post injury but no net effect after three weeks⁸

Complications:

1. Hematoma^{9a} (ileopsoas, rectus sheath^{9b}, arterial puncture sites, gut wall, in the CNS, and from failure to protect the patient from IM injection)
2. Hemorrhage from previously undiagnosed disease sites, (peptic ulcer, colonic CA, pyelonephritis, retroperitoneal tumor)
3. Enhanced bleeding tendency when anti-platelet aggregating agents are inadvertently prescribed (dipyridimole, ASA)
4. Controversial area: induction of priapism¹⁰

Administration:

1. Continuous
 - a. 5,000 u bolus then 1,200 ± 300 u/hr via infusion pump¹¹ NB. Heparin is denser than water and should not be placed in liter IV bottles for long-term drip therapy
2. Intermittent
 - a. 10,000 u q4hr × 24-36 hr, then 7,500 ± 2,500 u q4hr for pulmonary embolism¹²
 - b. 7,500 ± 2,500 u q4-6hr or 100 u/kg bolus and then 50 u/kg q2-4hr as standard treatment^{5, 24}
 - c. 5,000 u q6hr for intravascular coagulation¹³
 - d. 20,000 u/15% surface area burned as bolus, then 10,000 u q4hr × 1-2 days, then subq in severe burns⁴
3. Subcutaneous
 - a. 5,000 u 2hr preop., 24hr postop. and then q12hr × 5 days as prophylaxis for prevention of deep venous thrombosis^{14a, b, c}
 - b. 7,500 to 10,000 u q8hr or 10,000 to 15,000 u q12hr for therapeutic anticoagulation

Action:

1. In the presence of antithrombin III, thrombin is inactivated and fibrinogen to fibrin conversion prevented¹⁵
2. Heparin is a powerful inhibitor and destructive accelerator of activated Factor X
3. It prevents activation of Factor IX
4. It may block thrombin mediated platelet release of pharmacologically active amines

5. It clears plasma of chylomicrons in vivo

Laboratory control:

1. Coagulation time—2-3X control or near 30 minutes 1/2 hr prior to next dose or anytime if Rx continuous
2. Activated partial thromboplastin time (aPTT)—60 to 100 seconds^{16a,b}
3. Activated recalcification time—80-125 seconds¹⁷
4. Activated whole blood PTT—BaSon time (150-300 sec) or Celite time (140-200 seconds)^{18,19}
5. Plasma heparin assay (indirect) using aPTT—near 2 u/ml plasma²⁰
6. Dale-Laidlow coagulometer—near 2 1/2 to 3 minutes

Neutralization:

1. 50-75 mg protamine sulfate IV over 20 minutes and repeated in an hour if necessary or 10 to 15 mg/1,000 u heparin to be neutralized over 20-30 minutes. NB. Heparin effect not neutralized by transfusion

There is no single opinion concerning the optimal dose and interval of administration of heparin, nor on how often to monitor its effect or by what laboratory measurement. The problems in establishing such data can be readily understood when the variables involved are appreciated. The use of heparin, which contains additional as yet unrecognized contaminants with unknown biological activities, in a subject with his own personal coagulation-fibrinolytic interrelationship (and whose "normal range" of activity when not receiving anticoagulants is difficult to establish adequately) predicts that there will be significant degrees of responsiveness in large populations.^{21,22} While there is a relatively consistent response pattern to a given dose in an individual patient once this is established, that information is only relatively applicable to the next patient. In general, the drug effect depends on its concentration and half-life; the larger the dose, the longer the half-life. Because of heparin's protein binding, the anticoagulant effect persists longer than the drug's biological half-life can be measured.^{23,24} Constant anticoagulation mimicking that achieved during continuous infusion can be obtained by giving

the dose at shorter intervals, thereby insuring that the heparin plasma level never falls below a minimum effective anticoagulant plasma concentration. If that same dose is given at longer intervals, the plasma level during the last 1/2 to 1 hour of the interval span may well be below minimum effective levels. Whether a constant level in excess of minimal effective concentrations is essential for successful therapy or intermittent activity spikes alternating above and below minimal effective concentrations achieve the same end result is unsettled. There is strong feeling in the United States, however, that constant minimally effective concentrations or greater are at least crucial in the first one to two days of treatment of pulmonary embolism.

In using 5,000 u q4hr IV or other modest treatment schedules, the "clotting time" by whatever technique needs to be done prior to treating and then once a day or less thereafter to insure that the desired effect is being realized. In the higher dosage ranges, monitoring should be done daily or twice daily and on either dosage schedule within thirty minutes prior to the next dose. The type of test available varies according to local facilities, experience and bias, but the newer bedside whole blood PTT's and the activated recalcification times may offer better correlation for smoothness of treatment programs at this time. The popular PTT appears to perform well in some hospitals and not others, and frequently poorly correlates with standard coagulation times when performed simultaneously. When converting from one test to another, it is useful to do both until confidence can be transferred to the newer technique.

The response rate in venous thrombosis is greater than in arterial thrombosis, probably relating to the fact that arterial thrombi are composed largely of aggregated platelets with the coagulation mechanism playing a relatively minor role in initiation and propagation of the thrombus. Heparin remains as one of the major drugs in the treatment of thrombotic disease. Ancrod, the Malaysian pit viper extract, and reptilase, milked from South American pit vipers, can also prevent thrombosis by inducing a selective benign hypofibrinogenemia but are still investigational and in short supply. Two additional arms of antithrombotic treatment relate to (a) drugs that affect platelet aggregation and (b) fibrin dissolution with streptokinase or urokinase.

References

1. VIGRAN I. M.: Clinical Anticoagulant Therapy. Philadelphia, Lea & Febiger, 1965, p 29.
- 2a. EBERT R. V.: Potential of anticoagulant therapy in acute myocardial infarction. *Circ Supp* IV:271, 1969.
- 2b. RUSSEK H. I.: The myth of anticoagulant prophylaxis in myocardial infarction. *Geriatrics* 26:116, 1971.
3. Anticoagulants in acute myocardial infarction. Cooperative trial results. *JAMA* 225:724, 1973.
4. SALIBA M. J., et al: Large burns in humans—treatment with heparin. *JAMA* 225:261, 1973.
5. DEYKIN D.: The use of heparin. *NEJM* 280:937, 1969.
- 6a. NATELSON E. A., et al: Heparin induced thrombocytopenia. *Ann Int Med* 71:1121, 1969.
- 6b. EIKA C.: The platelet aggregating effect of eight commercial heparins. *Scand J Haemat* 9:480, 1972.
7. THOMPSON R. C.: Heparin osteoporosis. *J Bone & Joint Surg* 55A:606, 1973.
8. THOMPSON R. C., et al: Effects of heparin on wound healing. *Surg G & O* 134:22, 1972.
- 9a. MACON W. L., et al: Significant complications of anticoagulant therapy. *Surgery* 68:571, 1970.
- 9b. MANIER J. W.: Rectus sheath hematoma. *Am J Gastroen* 57:443, 1972.
10. DUGGAN M. L.: Heparin, a cause of priapism? *South Med J* 63:1131, 1970.
11. Management of thrombosis. Editorial, *Lancet* 2:361, 1971.
12. Pulmonary Thromboembolism. Edited by K. M. Moser and M. Stein. Year Book Medical Publishers, 1973, Chicago, Illinois.
13. PIERCE L. E.: Disseminated intravascular coagulation. *Am Fam Phys* 7:118, 1973.
- 14a. KAKKAR V. V., et al: Low doses of heparin in prevention of deep vein thrombosis. *Lancet* 2:669, 1971.
- 14b. NICOLAIDES A. N., et al: Small doses of subcutaneous sodium heparin in preventing deep venous thrombosis after major surgery. *Lancet* 2:890, 1972.
- 14c. GORDON-SMITH I. C., et al: Controlled trial of two regimens of subcutaneous heparin in prevention of postoperative deep-vein thrombosis. *Lancet* 1:1133, 1972.
15. Human Blood Coagulation, Haemostasis, and Thrombosis. Edited by R. Biggs. Oxford, Blackwell Scientific Publications, 1972.
- 16a. SPECTOR I., CORN M.: Control of heparin therapy with activated PTT. *JAMA* 201:157, 1967.
- 16b. BASU D., et al: A prospective study of the value of monitoring heparin treatment with the aPTT. *NEJM* 287:324, 1972.
17. RAY P. K., HARPER T. A.: Comparison of activated recalcification and PTT as controls for heparin therapy. *J Lab & Clin Med* 77:901, 1971.
18. BADEN J. P., et al: Precise measurement of heparin therapy. *Am J Surg* 124:777, 1972.
19. CONGDON J. E., et al: Monitoring heparin therapy in hemodialysis. *JAMA* 226:1529, 1973.
20. MARDER V. J.: Simple technic for the measurement of plasma heparin concentration during anticoagulant therapy. *Thromb et Diath Haemorr* 24:230, 1970.
21. WALTON P. L., et al: Heterogeneity of heparin. *Brit J Haemat* 12:310, 1966.
22. BANGHAM D. R., WOODWARD P. M.: A collaborative study of heparins from different sources. *Bull World Health Orgn* 42:129, 1970.
23. ESTES J. W.: Heterogeneity of the anticoagulant response to heparin. *J Clin Path* 25:45, 1972.
24. ESTES J. W.: Heparin therapy. *Int Med Digest*, p 33, January, 1971.

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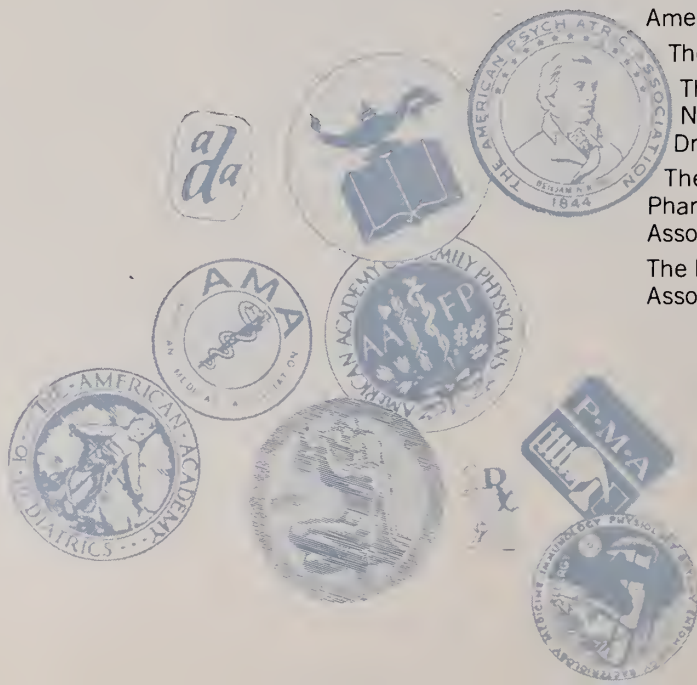
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Association



Joint Statement on Antisubstitution Laws and Regulations

The purpose of this statement is to affirm the support of the participating organizations for the laws, regulations and professional traditions which prohibit the unauthorized substitution of drug products.

Traditionally, physicians, dentists and pharmacists have worked cooperatively to serve the best interests of patients. Productive cooperation has been achieved through mutual respect as well as a common concern for the ideals of public service. This mutual respect has been reflected, in part, by joint support over the years for the adoption and enforcement of laws and regulations specifically prohibiting unauthorized substitution and encouraging joint discussion and selection of the source of supply of drug products. The basic principles of medical, dental and pharmacy practice are thus utilized and preserved in the interest of patient welfare.

The antisubstitution laws have not obstructed enhancement of the professional status of pharmacy any more than they have in and of themselves guaranteed absolute protection from unsafe drugs, or freed physicians, dentists and pharmacists from their responsibilities to patients. As a practical matter, however, such laws and regulations encourage inter-professional communications regarding drug product selection and assure each profession the opportunity to exercise fully its expertise in drug usage, to the advantage of patients.

Physicians and dentists should be urged to increase the frequency and regularity of their contacts with pharmacists in selection of quality drug products, recognizing that

economies to patients can be improved through such communication, taking into account the patients' needs. The pharmacist's knowledge of the chemical characteristics of drugs, their mode of action, toxic properties and other characteristics that assist in making drug selection decisions should be utilized to the fullest extent practicable by physicians and dentists in serving their patients.

Since drug product selection entails knowledge derived from clinical experience, the physician's and dentist's roles in product selection remain primary and do not permit delegation of decisions requiring medical and dental judgments. A broader role in therapy will evolve for pharmacists as improved understanding and cooperation among the professions continue to grow.

There has been no evidence that there are convincing reasons to modify or repeal existing laws and regulations prohibiting the unauthorized substitution of another drug product for the one specified by a prescriber. It is our belief that such laws and regulations merit the joint support of the medical, dental and pharmaceutical professions and the pharmaceutical industry.

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SCIENTIFIC ARTICLES

Pneumothorax During Respirator Therapy

JACK E. ZIMMERMAN, M.D., BURDETT S. DUNBAR, M.D. AND C. HERMAN KLINGENMAIER, M.D.

Abstract

Patients developing pneumothorax during respiratory support present a difficult diagnostic and therapeutic problem. The inability of the patient to communicate distress means that diagnosis will depend upon anticipation and interpretation of clinical signs. The complication is successfully managed by emergency decompression and tube thoracostomy. Continuing respiratory support potentiates air leakage and delays sealing. Therefore, tube thoracostomy may be needed for prolonged periods and premature clamping or removal will result in recurrent pneumothorax.

Introduction

An increasing number of patients with acute reversible respiratory failure are being effectively supported with mechanical ventilators. Although this therapy has decreased the mortality of respiratory failure it is not without hazards, including pneumothorax occurring during mechanical ventilation. Among 430 patients receiving ventilator support for more than 12 hours in our Intensive Care Unit during the past two years, we have encountered this complication in 15.¹ The following is a review of the pathogenesis and recognition of pneumothorax in patients on ventilators with suggestions for its prevention and management.

Pathogenesis

In spontaneous pneumothorax associated with rupture of apical blebs

the pathogenesis appears to be analogous to the rupture of an over-inflated balloon. A similar mechanism exists in patients on respirators when emphysematous blebs or infected lung parenchyma are ruptured by the application of positive pressure to the airway. Macklin² stressed the mechanism of rupture of alveoli with sequential dissection of gas along pulmonary vascular sheaths into the mediastinum, and along fascial planes into the subcutaneous tissues, the retroperitoneal space, or the pleural cavities.

The application of positive pressure to the airway itself is a cause of a pneumothorax.^{3,4} Peak inflation pressures greater than 80 cm. H₂O are definitely dangerous, pressures of 30 to 80 cm. H₂O are potentially dangerous, and pressures less than 25 cm. H₂O are safe.⁵

In our own experience one or more diseases predisposing to pneumothorax were frequently present in patients who developed this complication during respirator therapy. Eleven of our 15 patients (73%) had such diseases. These included emphysema in five patients, necrotizing pneumonia in four, status asthmaticus in one, and both emphysema and necrotizing pneumonia in one patient. These processes seemed more closely related to the genesis of pneumothorax than peak or mean airway pressure, or the use of positive end expiratory pressure (PEEP).

Even more important were preventable iatrogenic causes of pneumothorax. Steier et al⁶ report a 70% increase in the incidence of pneumo-

thorax as a result of iatrogenic factors. Among our patients subclavian vein catheterization was the most important iatrogenic factor and caused pneumothorax in three patients. A high percentage of the complications from this procedure can be related to its indiscriminate use and insertion by inexperienced, unsupervised personnel under hazardous circumstances. We believe that patients on respirators or patients with obstructive airway disease constitute such a hazard. In either case the lung apices may be hyperinflated and forced into an abnormally close proximity to the subclavian vein. More peripheral sites or the internal jugular vein are safer routes for central venous catheterization in this situation. If catheterization of the subclavian vein is necessary in a patient on a respirator, ventilatory assistance should be stopped momentarily during insertion in order to decrease the risk of pneumothorax.

Clinical Findings

The diagnosis of pneumothorax during respirator therapy is difficult, especially if this complication is not anticipated. The manifestations can differ from those of the spontaneously breathing patient and the consequences can be more rapidly life threatening. The patient may be unable to communicate distress because of an artificial airway, heavy sedation, or the use of muscle relaxants. Thus, diagnosis depends on the alertness of the attending physician and nurse in interpreting clinical signs.

PNEUMOTHORAX DURING RESPIRATOR THERAPY

ZIMMERMAN, DUNBAR AND KLINGENMAIER

Sixty-five percent of our patients presented with acute cardiorespiratory distress associated with tension pneumothorax. Tachypnea, loss of synchrony with the respirator, precipitous rises in peak inspiratory pressure, hypotension, tachycardia, diaphoresis, and evidence of cardiac arrhythmia were frequent and relatively non-specific findings. The diagnosis was suggested by the absence or decrease of breath sounds in one hemithorax, development of subcutaneous emphysema, presence of cardiac or tracheal deviation with confirmation by radiographic examination or air aspiration.

Clinical or radiographic evidence of subcutaneous emphysema, pneumomediastinum, or loculated intrapleural air are important signs that may precede the occurrence of pneumothorax. In six of our patients these findings preceded the development of pneumothorax by periods of four hours to three days. Whenever air is found in the wrong place one should be alerted to the possibility of pneumothorax since respirator therapy will tend to force more gas through the site of rupture and perhaps ultimately into one or both pleural spaces.

Pneumothorax complicating respirator therapy is not always a dramatic clinical event. In three of our patients loculated or small pneumothoraces were only detectable by chest x-ray. Even on retrospective examination no clinical or physiologic changes were detectable.

Management

A patient who already requires respirator support can ill afford the additional insult of pneumothorax. Therefore, prompt recognition and treatment are vital. When tension pneumothorax is diagnosed immediate relief of tension by air aspiration is indicated. For emergency decompression we prefer to insert any of the

commonly available plastic intravenous catheters. The catheter is inserted into the pleural space between the third and fourth ribs at the anterior axillary line. A 3-way stopcock and 50 cc. syringe are used for air aspiration. This system allows continuous air aspiration without the risk of additional lung damage caused by needle lacerations as the lung reexpands, and provides time for tube thoracostomy to be performed under proper conditions.

All patients who develop pneumothorax during respirator therapy should have tube thoracostomy with 10 to 20 cm. H₂O pleural suction regardless of clinical symptoms. Expectant management of small asymptomatic or loculated pneumothorax is associated with a high risk of increasing lung volume loss or developing tension pneumothorax because of the respirator's tendency to force more gas into the pleural space. This sequence of events occurred in two of our patients who were not immediately treated by tube thoracostomy.

Tube thoracostomy and pleural suction successfully reexpanded the lung in all of our patients. Problems with continued respirator management were rare, since air leakage was usually moderate. When large air leaks are encountered considerable difficulties with respirator management can occur.⁷ Successful treatment depends on the recognition by the managing physician that the respirator, the patient's pleural space, and the tube thoracostomy are an interrelated system. Thus, continued application of positive pressure to the airway will increase the tendency for air leak and decrease the ease of reapproximating pleural surfaces.

Since respirator therapy promotes continued air leakage a need for intrapleural suction for longer than the two to four day period required in uncomplicated spontaneous pneumo-

thorax^{8,9} should be expected. Our patients continued to leak air for an average of 11 days and required tube thoracostomy for an average of 14 days. Throughout this period of time adequate lung expansion and tube patency must be assured. Observing air leakage, which may be subtle and evident only during the peak of respirator pressure or when suction is temporarily increased, is critically important. Although continued respirator support may be a clinical necessity it is desirable to minimize airway pressure and wean the patient at the earliest possible moment so that pleural symphysis can be achieved.

Chest tubes should remain connected to suction until no air leak and full lung expansion have been present for at least 48 hours. The lung should remain fully expanded following a one day trial of underwater seal drainage without suction prior to tube clamping and removal.

Our experience has led us to develop an extremely conservative attitude regarding the clamping or removal of chest tubes in respirator patients. The result of premature clamping or removal of chest tubes in these patients can be a rapidly fatal tension pneumothorax.

Summary

Pneumothorax is a frequent complication in respirator patients with pre-existing pulmonary disease. The usual clues, such as chest pain and dyspnea, are not present. Non-specific cardiopulmonary signs of deterioration may be the only change, so radiological examination must be done to diagnose pneumothorax. Prolonged chest tube drainage is usually required for successful management.

References

1. ZIMMERMAN, J., et al: Management of patients developing subcutaneous emphysema, pneumomediastinum and pneumothorax during respirator therapy. In press.
2. MACKLIN, M., MACKLIN, C: Malignant interstitial emphysema of the lungs and mediastinum. *Medicine*, 1944, 23, 281.
3. JOANNIDES, M., TSOULOS, E: The etiology of interstitial and mediastinal emphysema. *Arch. Surg.*, 1930, 21, 333.
4. MACKLIN, C.: Pneumothorax with massive collapse from experimental local overinflation of the lung substance. *Canad. Med. Assoc. J.*, 1937, 36, 414.
5. NENNHAUS, H., et al: Alveolar and pleural rupture, hazards of positive pressure respiration. *Arch. Surg.*, 1967, 94, 136.
6. STEIER, M., et al: Iatrogenic causes of pneumothorax. *NY State J. Med.*, 1973, 73, 1296.
7. ZIMMERMAN, J., et al: Bronchopleural fistula complicating therapy with PEEP. *Chest*, 1973, 64, 526.
8. KLASSEN, K: Treatment of spontaneous pneumothorax. *JAMA*, 1962, 182, 1.
9. MILLS, M., BAISCH, B: Spontaneous pneumothorax, a series of 400 cases. *Ann. Thorac. Surg.*, 1965, 1, 286.

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THE VIEW BOX

Prepared by
The Department of Radiology
Washington Hospital Center

One (1) year old black male child with painful swollen hands.

(for diagnosis see page 171)



Response of Asthmatic Airways to Intravenous Bradykinin and Histamine

HAROLD H. NEWBALL, M.D.

Abstract

This work explored the response of asthmatic airways to intravenous bradykinin and histamine. The substances were rapidly injected intravenously and measurements made of the respiratory system resistance (Rrs), closing volume (CV), forced vital capacity (FVC), expiratory volume in the first second (FEV₁), FEV₁/FVC (FEV₁%), maximal midexpiratory flow (MMF), and peak flow (PF). Bradykinin decreased Rrs (−18%) and CV (−12%), and increased FEV₁ (9%), FEV₁% (8%), MMF (23%), and PF (9%) significantly, but did not change the FVC. The data are consistent with results from animal studies which indicate that bradykinin may release adrenaline (or other agents) that cause secondary effects, such as bronchodilation. Histamine increased Rrs (24%) and CV (53%), and decreased FVC (−20%), FEV₁ (−14%), and PF (−16%) significantly. Thus, in the asthmatic intravenous histamine constricts both large and small airways. The data suggest that intravenous bradykinin has no major bronchoconstricting effect. It may, however, have a role in regulating airway smooth muscle tone by releasing other agents.

Introduction

Bradykinin and histamine have been implicated as mediators of the acute

asthmatic attack¹. The 10-fold elevation above normal of blood kinin reported in severe asthmatics suggests that kinin may be released in the asthmatic attack². Aerosolized bradykinin significantly decreases peak expiratory flow in asthmatics but not in normal persons³. It is not clear, however, whether this reaction is mediated by bradykinin or simply represents an overall bronchial hyperactivity of the asthma patient to an irritating stimulus. Aerosolized histamine causes bronchoconstriction in normal subjects as well as in asthmatics, although asthmatics are more sensitive⁴.

Reports of the respiratory effects of intravenous histamine in normal man have been conflicting; some investigators observe no significant effects while others observe a decrease of specific airway conductance^{5,6}. We are unaware of any data on the respiratory effects of intravenous bradykinin. The conflicting data on the importance of bradykinin and histamine as mediators and the absence of information on bradykinin given intravenously led to this study. We also attempted to determine the probable site of action of these agents.

Methods

Subject. Four men and 6 women, ages 18 to 47, were hospitalized in the Clinical Center, N.I.H., during the

three days of the study. They all reported a history of extrinsic bronchial asthma, and on pulmonary function studies had reversible airways obstruction. There was no evidence of any other lung disease. Patients were not given bronchodilators nor any other drugs for approximately 24 hours prior to the studies. The severity of the disease was variable, some having perennial symptoms while others had only seasonal symptoms. At the time of the studies they were at their usual asymptomatic state.

Drugs. Bradykinin, purchased from Schwarz-Mann, Dickinson and Company was synthesized by the solid phase technique of Merrifield⁷. Its purity was confirmed by us with amino acid analysis and chromatography, then packaged, lyophilized in siliconized bottles, and diluted with normal saline just before use, to a concentration of 25 µg/ml. Histamine acid phosphate U.S.P. was purchased from Eli Lilly Company. A placebo of 0.9% saline of a volume equal to that of bradykinin and histamine was used for each control.

Equipment. The oscillator resistance unit used in these studies has been described⁸. It was operated at a constant pressure of 2 cm H₂O and a frequency of 3 Hz. Closing volume was measured as described by Anthonisen, *et al.*⁹. Nitrogen was measured by a rapid analyzer (Med-Science, Model 505), and volume change with a Wedge

INTRAVENOUS BRADYKININ AND HISTAMINE IN ASTHMA

NEWBALL

Spirometer (Med-Science, Model 570), the outputs of which were plotted on an X-Y recorder (Hewlett-Packard Model 7034A). Forced vital capacity (FVC) was measured with a Stead-Wells Spirometer (Warren Collins) which is interfaced to a Nova 1200 computer so that all measurements are automated.

Protocol. On day one routine pulmonary function, closing volume (CV) measurements and respiratory system resistance (Rrs) were done in order to familiarize subjects with the equipment. On day two an intravenous (I.V.) infusion of normal saline was started in a forearm vein and all injections were made via this route. Rrs was measured after the rapid injection of the placebo. The same measurement procedure was followed for bradykinin, subjects receiving 1 $\mu\text{g}/\text{Kg}$ body weight. Rrs was measured continuously for two minutes starting at the time of each injection. The average Rrs for all measurable breaths was determined for 30-second intervals. At the end of each Rrs determination their inspiratory capacity was measured. We then measured CV after similar placebo, and bradykinin injections, starting approximately 30 seconds after the respective I.V. injections. Forced vital capacity after placebo and bradykinin injections was next determined, with measurements of vital capacity (FVC), expiratory volume in the first second (FEV_1), FEV_1/FVC ($\text{FEV}_1\%$), maximal mid-expiratory flow (MMF) and peak flow (PF). Five FVC measurements at 30-second intervals after the placebo were used as controls for the respective five post-bradykinin observations. The three injections of bradykinin were about 30 minutes apart. On day three, the same observations were made to study the effects of histamine acid phosphate, with injections of 0.5 $\mu\text{g}/\text{Kg}$ body weight.

Subjects were unaware of which

drug they were receiving on a particular day, or that they would receive a placebo injection. The data were analyzed by the t test for paired observations.

Results

In all subjects, intravenous bradykinin and histamine produced systemic reactions, while placebo produced no reaction in any subject. Bradykinin and histamine induced similar systemic symptoms, however, the histamine induced symptoms persisted for a longer period of time. The most frequent symptom was a throbbing headache, the degree of which varied. Less frequent symptoms included breathlessness, tightness in the chest, and palpitations. The bradykinin induced symptoms of respiratory distress were transient, generally persisting for less than a minute. Inspiratory capacity comparisons for bradykinin or histamine versus placebo were not significantly different.

Bradykinin. The average Rrs for 30-second intervals significantly decreased with bradykinin compared to the placebo (Fig. 1, Table 1). The average Rrs decrease for the first, second, third and fourth intervals were -2%, -18%, -15%, and -6%, respectively. The closing volume of eight of the 10 asthmatics decreased (-12%, $p = .05$). There was no significant change of the FVC, however, there were significant increases of the FEV_1 (9%, $p < .02$), FEV (8%, $p < .05$), MMF (23%, $p < .02$), and PF (9%, $p < .01$, Table 2).

Histamine. Average Rrs, for 30-second intervals, significantly increased with histamine when compared to the placebo (Fig. 1, Table 1). The average Rrs increase for the first, second, third, and fourth intervals were 12%, 24%, 15%, and 17% respectively. Histamine caused an increase of the CV (53%, $p < .01$) in all subjects. There

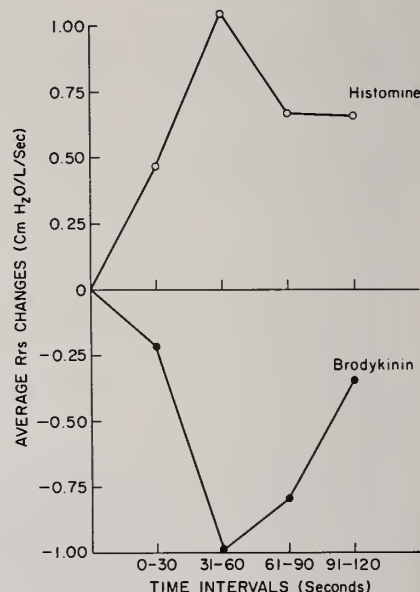


FIG. 1. Effects of intravenous bradykinin and histamine on the Rrs of asthmatics. Histamine increases the resistance (bronchoconstriction) while bradykinin decreases the resistance (bronchodilation).

were decreases of the FVC (-20%, $p < .025$), FEV_1 (-14%, $p < .05$), and the PF (-16%, $p < .05$). After 90 seconds, there were no significant bradykinin or histamine induced changes from the placebo for the FVC, FEV_1 , $\text{FEV}_1\%$, MMF, or PF.

Discussion

Airway resistance represents the major component of Rrs¹⁰, and large airways (internal diameter (ID) > 2 mm) contribute at least 90% of the airway resistance¹¹. Thus, the measurement of Rrs is a relatively sensitive index of large airway resistance changes. Closing volume is reported to be particularly sensitive to changes of the small airways (ID < 2 mm)¹². The FVC might confirm a gross change, even though it would not pinpoint the site of drug action.

There is some evidence that normal

airways are relatively hyposensitive to bradykinin. Bhoola, *et al.*¹³ reported that preparations of human bronchi recovered from lungs excised for carcinoma did not respond *in vitro* to bradykinin in concentrations up to 667 $\mu\text{g/ml}$. These same specimens contracted when exposed to acetylcholine in concentrations of 0.2 to 0.67 $\mu\text{g/ml}$ and to histamine in concentrations of 0.067 to 0.67 $\mu\text{g/ml}$. Other investigators report a wide range of sensitivity of human bronchial smooth muscle to bradykinin *in vitro*¹⁴. Asthmatics when given intravenous bradykinin significantly decreased the Rrs and CV, while increasing the FEV₁, FEV₁%, MMF and PF. Thus, asthmatics showed bronchodilation of both large and small airways. Bradykinin is known to release adrenaline from the cat adrenal medulla¹⁵, and also to release prostaglandins¹⁶. The data suggest that bradykinin releases adrenaline and possibly prostaglandins E₁ and E₂ which lead to secondary bronchodilation.

Histamine caused significant increases of the Rrs and CV, with concomitant decreases of the FVC, FEV₁, and PF. Thus, histamine caused constriction of both large and small airways. Both bradykinin and histamine release adrenaline from the adrenal medulla of animals^{15,17}. Histamine has long been used in man as a provocative test for the diagnosis of pheochromocytoma, the pressor response presumably being secondary to adrenaline release from the tumor. Even though both agents probably also release adrenaline in the asthmatic, he responds oppositely to them (Fig. 1), bradykinin causing a bronchodilation but histamine causing bronchoconstriction. This difference in response is most likely due to a bronchoconstrictor effect of histamine, which is later counteracted by adrenaline release, so that the airways then dilate and return toward their initial state within a few

TABLE 1: Effects of intravenous bradykinin and histamine on the Rrs of asthmatics.
Values represent average Rrs differences of bradykinin or histamine minus saline placebo for 30 second intervals (Cm H₂O/L/Sec.).

Time (sec.)	Bradykinin			Histamine		
	Mean	SE	P	Mean	SE	P
0-30	-.22	.20	N.S.	.47	.45	N.S.
31-60	-.99	.27	<.01	1.05	.34	<.05
61-90	-.80	.41	.05	.67	.26	<.05
91-120	-.35	.32	N.S.	.66	.29	.05

minutes. Bradykinin in contrast, probably causes no significant bronchoconstriction, so the airways dilate earlier and to a greater degree with adrenaline release.

Bradykinin, *in vivo*¹⁸ and *in vitro*¹³ has no major constricting effect on normal human airways. There is probably no "mediator" effect on the airways of asthmatics. If the bronchodilation seen in the asthmatic is not secondary to adrenaline (or other bronchodilator) release, then the response of asthmatic airways to intravenous bradykinin is bronchodilation, and not bronchoconstriction. The *in vitro* studies¹³ suggest that bradykinin has no intrinsic bronchodilating effect, consequently it is more likely that bradykinin releases a bronchodilating agent. Thus, the decreased peak expiratory flow reported in asthmatics given aerosolized bradykinin³ most likely represents not a bradykinin-mediated response, but rather the overall bronchial hyperreactivity of asthmatic patients to irritating stimuli.

The reported elevated blood kinin in severe asthmatics² could be detrimental in two respects. If bradykinin releases adrenaline in asthmatics as suggested by the data, an elevated blood kinin level might cause a continuous release of adrenaline which may contribute to the "epinephrine fast" condition seen during the severe asthmatic attack. We have previously presented suggestive evidence for alveolar

duct constriction in man during bradykinin infusion¹⁸. If bradykinin is a significant mediator of the asthmatic attack, its effects are probably exerted at the level of the alveolar duct. It is unlikely that alveolar duct constriction would increase the work of breathing sufficiently to account for the degree of respiratory distress experienced by the asthmatics. Alveolar duct constriction may lead to distortion or stimulation of receptors, causing the respiratory distress as described by the asthmatics.

Summary

Bradykinin and histamine have been considered possible mediators of the acute asthmatic attack. This study measured the effects of each given intravenously. Intravenous histamine constricted both large and small airways; bradykinin had no major bronchoconstricting effect. Rather, it caused physiological effects suggestive of bronchodilation, probably at the level of the alveolar duct, through release of a dilating agent.

Acknowledgements

The author gratefully acknowledges the advice and encouragement of Drs. Claude Lenfant, Harry Keiser, and John Pisano, and the skillful assistance of Mr. Charles Berkovich.

INTRAVENOUS BRADYKININ AND HISTAMINE IN ASTHMA

NEWBALL

TABLE 2: Effects of intravenous bradykinin and histamine on pulmonary function in asthmatics. Values represent percentage volume change of bradykinin (B) minus saline (S) placebo (B-S/S) X 100 or histamine (H) minus saline placebo (H-S/S) X 100 at 30 second intervals.

Time (sec.)		Bradykinin			Histamine		
		Mean	SE	P	Mean	SE	P
FVC	30	-1.63	1.61	N.S.	-20.20	6.23	<.025
	60	2.90	2.54	N.S.	-6.15	3.18	N.S.
	90	4.54	3.27	N.S.	2.63	6.46	N.S.
FEV ₁	30	6.06	3.90	N.S.	-14.22	5.52	<.05
	60	9.01	3.16	<.02	-0.93	3.30	N.S.
	90	5.95	4.27	N.S.	2.10	5.19	N.S.
PF	30	-0.27	4.23	N.S.	-16.05	6.23	<.05
	60	8.52	3.56	<.05	7.30	2.94	.05
	90	8.67	2.37	<.01	.97	8.87	N.S.

References

1. AAS, K.: Biochemical mediators of immediate hypersensitivity reactions and bronchial asthma. In: *The Biochemical and Immunological Basis of Bronchial Asthma*. Charles C Thomas, Springfield, 1972, 115.
2. ABE, K., WATANABE, N., KUMAGAI, N., MOURI, T., SEKI, T., YOSHINAGA, K.: Circulating plasma kinin in patients with bronchial asthma. *Experientia*, 1967, 23, 626.
3. VARONIER, H. S., PANZANI, R.: The effect of inhalations of bradykinin on healthy and atopic (asthmatic) children. *Int. Arch. Allergy*, 1968, 34, 293.
4. SIMONSSON, B. G., JACOBS, F. M., NADEL, J. A.: Role of autonomic nervous system and the cough reflex in the increased responsiveness of airways in patients with obstructive airway disease. *J. Clin. Invest.* 1967, 40, 1812.
5. BOUHUYS, A., JONSSON, R., LICHTNECKERT, S., LINDELL, S.-E., LUNDGREN, C., LUNDIN, G., RINGQUIST, T. R.: Effects of histamine on pulmonary ventilation in man. *Clin. Sci.* 1960, 19, 79.
6. EPSTEIN, S. W., WARRELL, D. A., ROBERTSON, D. G., NEWTON-HOWES, J., FLETCHER, C. M.: The effect of intravenous histamine on specific airway conductance in patients with airway obstruction and in normal subjects. *Resp.* 1970, 27, 201.
7. MERRIFIELD, R. B.: Solid phase peptide synthesis. II. The synthesis of bradykinin. *J. Am. Chem. Soc.* 1964, 86, 304.
8. GOLDMAN, R., KNUDSON, R. J., MEAD, J., PETERSON, N., SCHWABER, J. R., WOHL, M. E.: A simplified measurement of respiratory resistance by forced oscillation. *J. Appl. Physiol.* 1970, 28, 113.
9. ANTHONISEN, N. R., DANSON, J., ROBERTSON, P. C., ROSS, W. R. D.: Airway closure as a function of age. *Respir. Physiol.* 1969/70, 8, 58.
10. MEAD, J.: Mechanical properties of lungs. *Physiol. Rev.* 1961, 41, 281.
11. MACKLEM, P. T., MEAD, J.: Resistance of central and peripheral airways measured by a retrograde catheter. *J. Appl. Physiol.* 1967, 22, 395.
12. MCCARTHY, D. S., SPENCER, R., GREENE, R., MILIC-EMILI, J.: Measurement of "closing volume" as a simple and sensitive test for early detection of small airway disease. *Am. J. Med.* 1972, 52, 747.
13. BHOOLA, K. D., COLLIER, H. O. J., SCHACHTER, M., SHORLEY, P. G.: Actions of some peptides on bronchial muscle. *Brit. J. Pharmacol.* 1962, 19, 190.
14. SIMONSSON, B. G., SKOOGH, B.-E., BERGH, N. P., ANDERSSON, R., SVEDMYR, N.: *In vivo* and *in vitro* effect of bradykinin on bronchial motor tone in normal subjects and patients with airways obstruction. *Respiration*, 1973, 30, 378.
15. FELDBERG, W., LEWIS, G. P.: The action of peptides on the adrenal medulla. Release of adrenaline by bradykinin and angiotensin. *J. Physiol.* 1964, 171, 98.
16. MONCADA, S., FERREIRA, S. H., VANE, J. R.: Does bradykinin cause pain through prostaglandin production. Report on Fifth International Congress on Pharmacology. Albert J. Phiebig, Inc., New York, 1972, 160.
17. STASZEWSKA-BARCZAK, J., VANE, J. R.: The release of catecholamines from the adrenal medulla by histamine. *Brit. J. Pharmacol.* 1965, 25, 728.
18. NEWBALL, H. H., KEISER, H. R.: Relative effects of bradykinin and histamine on the respiratory system of man. *J. Appl. Physiol.* 1973, 35, 552.

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Immunologic Studies in Nitrofurantoin Induced Pulmonary Disease

ROBERT A. GOLDSTEIN, M.D. AND BERNARD W. JANICKI, PH.D.

Abstract

Nitrofurantoin induced lung disease may occur more often than clinically recognized owing to the lack of specific diagnostic tests. We have presented preliminary evidence to support the concept that acute pulmonary reactions to nitrofurantoin may be associated with the presence of specific cellular reactivity to the drug even in the absence of a specific antibody response. Because provocation testing in suspected cases is potentially hazardous, it is hoped that extension and confirmation of these findings may lead to the development of a laboratory aid for the diagnosis of drug induced lung disease.

Introduction

Drug induced pulmonary diseases have been the subject of several recent reviews¹⁻³ and numerous agents now have been recognized to cause serious and occasionally fatal illnesses. Because confirmatory laboratory tests are usually lacking, the correct clinical diagnosis is usually reached by a careful history combined with the knowledge that certain drugs may produce characteristic pulmonary diseases. For example, although it has been known since 1962⁴ that nitrofurantoin could produce a severe pulmonary illness, to date only provocation tests have been successfully used to confirm the suspected clinical

diagnosis⁵. However, because such challenges may be hazardous, several investigators⁶⁻⁸ have utilized *in vitro* immunologic methods in an attempt not only to elucidate the pathogenesis of the disease but also to develop laboratory tests for the detection of drug reactions.

We have recently had the opportunity to perform immunologic studies in a patient who had experienced a severe pulmonary reaction to nitrofurantoin. In addition to re-emphasizing the importance of this clinical syndrome, we have obtained suggestive evidence that *in vitro* studies of lymphocytes from such individuals may provide laboratory confirmation for the clinical diagnosis.

Materials

Study Subject

Mrs. B. P., a 54-year old retired secretary, was admitted to the George Washington University Hospital on July 10, 1973, because of the sudden onset of shortness of breath and chest pain during the preceding 24 hours. She was in her usual state of health until one week prior to admission when she received nitrofurantoin therapy for cystitis. The medication was discontinued two days prior to admission and one day later she awoke with the sudden onset of shortness of breath and palpitations. This was later associated with substernal pleuritic

chest pain, fever, headache, non-productive cough and weakness.

Past medical history included essential hypertension, aortic insufficiency and stenosis, and occasional episodes of angina pectoris and palpitations. These conditions were quite stable and well controlled with a thiazide diuretic, isosorbide dinitrate, and propranolol.

Physical examination at the time of admission revealed an anxious woman in obvious respiratory distress. Vital signs included a temperature of 37.6°C, a regular pulse at 120, a blood pressure of 140/80 and labored respiration at a rate of 24. Positive findings included grade 2 of 6 systolic and diastolic murmurs and bibasilar rales. There was no calf tenderness and Homan's sign was negative.

Laboratory studies showed a hematocrit of 43, a white blood count of 20,800 with predominant neutrophilia, and 2% eosinophils (subsequently 6%). Arterial blood gases drawn while the patient was breathing nasal oxygen showed Pa O₂ 93 mm Hg, Pa CO₂ 35 mm Hg, and pH 7.39. An electrocardiogram showed sinus tachycardia and findings compatible with an old anterior wall myocardial infarction. The initial AP chest x-ray (Fig. 1) showed a diffuse interstitial pattern and slight cardiomegaly. She improved markedly with supportive care during the next 24 hours and a repeat x-ray more clearly demonstrated the diffuse reticular nodular infiltrate. Her physician concluded at

IMMUNOLOGIC STUDY IN NITROFURANTOIN LUNG DISEASE

GOLDSTEIN AND JANICKI



FIG. 1. AP Chest Roentgenogram on Admission.

this time that she might be suffering from a pulmonary reaction to nitrofurantoin. Five days after admission, the interstitial pattern had cleared and bilateral pleural effusions developed (Fig. 2). Her subsequent hospital course was uneventful.

Owing to the complexity of her underlying medical diseases and the severity of her clinical presentation, the initial diagnostic impressions included pulmonary embolism and myocardial infarction. The realization that her chest x-ray in fact demonstrated a diffuse interstitial pattern combined

with the knowledge that nitrofurantoin might produce this clinical picture led to the conclusion that she may have experienced a drug induced pulmonary disease.* An attempt to confirm this diagnosis by provocation testing was considered too hazardous to perform.

Control Subjects

Nine persons served as control subjects. Five were healthy and had never received nitrofurantoin. Three had received nitrofurantoin without

difficulty four months prior, two weeks prior, and during study. One person had experienced an acute febrile flu-like illness and skin rash while taking the drug 18 months previously. Oral challenge at that time reproduced the same clinical illness in six to eight hours without evidence of pulmonary involvement.

Methods

Cellular Studies

The *in vitro* blastogenic response of cultured peripheral blood lymphocytes was measured by tritiated thymidine incorporation⁹. This technique was modified to include the *in vitro* exposure of lymphocytes to varying concentrations of nitrofurantoin. In addition to cultures using autologous plasma, "cross-over" experiments were performed using the subject's own cells and homologous plasma from a healthy control. Conversely, cells from healthy controls and homologous plasma from the study subjects were examined. These latter experiments were designed to evaluate the influence of plasma constituents upon cell cultures. Blastogenesis was expressed as a stimulated to control (S/C) ratio which was calculated by dividing the mean disintegrations per minute of stimulated (S) cultures by that of the unstimulated (C) cultures.

Humoral Studies

Sera were analyzed by a primary binding test for anti-nitrofurantoin reactivity. Triplicate tubes each received 0.10 ml of undiluted serum and 0.5 μ g of nitrofurantoin-hydantoin-2-¹⁴C† in 0.10 ml of borate buffer (pH 8.4). They were incubated overnight at 5°C after which the serum globulins were precipitated by adding 0.20 ml of saturated ammonium sulfate to each tube. The mixtures were kept at 5°C for 30 minutes and then the precipi-

tates were sedimented by centrifugation at 2,000 X G for 30 minutes at 5°C. The precipitates were resuspended and washed once in 50% ammonium sulfate and dissolved in 1 ml of NCS solubilizer; 10 ml of Spectrafluor were added to each sample for radioactivity measurements in a liquid scintillation system. Triplicate 0.5 µg samples of ¹⁴C-nitrofurantoin were diluted in solubilizer and fluor and counted to determine the amount of radioactivity added to each serum sample. Anti-nitrofurantoin reactivity in the sera was expressed as the percentage of the radioactivity added which was precipitated with the serum globulins.

Results

Results of cellular and humoral studies are summarized in Table 1. When compared to control subjects and other nitrofurantoin-treated patients, patient B. P. exhibited significant cellular reactivity to nitrofurantoin. Her response was sustained, if not increased, approximately 3 months after her hospitalization. In contrast, the patient who had previously experienced a hypersensitivity reaction exhibited minimal, probably insignificant, lymphocyte blastogenesis with nitrofurantoin, as did the three other patients who were treated without adverse reactions. It should be mentioned that cells from patient B. P. were tested against various concentrations of nitrofurantoin in preliminary experiments; maximal blastogenesis was obtained with 1 and 5 µg/ml concentrations; less reactivity was noted with 10 µg, and 25 µg concentrations appeared to be cytotoxic. The serologic test results provided no evidence either directly from the binding test or indirectly from the "plasma cross-over" cellular studies for the presence of anti-nitrofurantoin humoral responses in any of the treated subjects. Similarly, immuno-



FIG. 2. PA Chest Roentgenogram 5 Days Later.

diffusion tests for precipitating antibodies against nitrofurantoin were negative.

Discussion

Acute pulmonary reactions to nitrofurantoin are characterized by the sudden onset of chills, fever, cough and dyspnea usually occurring within hours or days following the initiation of therapy. This pattern also may be associated with skin rashes and eosinophilia. Such reactions do not have to follow the initial exposure to the drug but may occur after several courses of

therapy. Once identified, however, oral provocation testing may reproduce the entire clinical illness within three to eight hours. A chest roentgenogram may show a diffuse interstitial pattern, with predominant lower lobe involvement; localized infiltrates, pleural effusions, and alveolar filling patterns with Kerley B lines also occur. Resolution of the x-ray changes usually occurs within 48-72 hours after cessation of therapy. Adjunctive therapy with corticosteroids seems efficacious in some instances but is apparently unnecessary. Chronic pulmonary reactions following prolonged

IMMUNOLOGIC STUDY IN NITROFURANTOIN LUNG DISEASE

GOLDSTEIN AND JANICKI

TABLE 1: Comparison of Cellular and Humoral Immune Reactivity to Nitrofurantoin in Treated and Control Subjects

Group	# Subjects	Cellular (S/C Ratio)	Humoral (% Binding)
Nitrofurantoin			
Pneumonia 7/23/73	1	7.6	2.9
10/5/73		19.5	2.8
Hypersensitivity Reaction	1	1.5	3.0
Without Reactions	3	0.6	3.4
		0.8	4.0
		0.8	4.2
Controls	5	0.4	2.6
		0.2	3.5
		0.8	2.9
		0.8	3.5
		0.5	3.5

exposure to nitrofurantoin may result in interstitial fibrosis which is similar in most respects to the "idiopathic" variety, and may be irreversible^{10,11}. These reactions may occur without regard to age, sex, race or other factors; however, there appears to be an increased incidence among postmenopausal white women perhaps related to an increased likelihood of exposure to the drug in this group.

More common allergic manifestations of nitrofurantoin hypersensitivity include macular, maculopapular and urticarial skin reactions, pruritus, and drug fever. Many patients have described a flu-like illness with respiratory symptoms, but chest roentgenograms were unavailable to confirm pulmonary involvement. Combining allergic reactions and toxic side effects, an overall reaction rate of 9.2% was found in one review¹² which represented an approximately three-fold greater rate when compared with a similar group of patients receiving sulfonamides.

Pulmonary reactions to nitrofurantoin may be associated with significant morbidity and lead to confusion in

differential diagnosis^{13,14}. This problem is well illustrated by the present case. Initially this patient was thought to have experienced an episode of pulmonary embolism. The rapid clinical defervescence combined with follow-up observation and immunologic studies have convinced us that she indeed manifested a pleuropneumonic reaction to nitrofurantoin.

Although unequivocal proof for an immunologic basis for pulmonary sensitivity to nitrofurantoin is lacking, the clinical features suggesting that it is immunologically mediated include: (1) fever and eosinophilia during acute episodes, (2) reproduction of the entire syndrome within hours after challenge with the drug in sensitive people, and (3) rapid clearing of the pulmonary infiltrates after withdrawal of the drug. Because these features are similar to other acute pulmonary reactions mediated by antigen-antibody complexes, nitrofurantoin induced lung disease has been presumed to occur in a similar manner¹⁵. Unfortunately, attempts to demonstrate the responsible antibody by several techniques^{5, 8} including the

sensitive primary binding test reported here have failed. An alternate view has been provided recently by Pearsall and co-workers⁸ to support the role of delayed type hypersensitivity or cell mediated immune responses in the pathogenesis of nitrofurantoin induced pneumonia. Lymphocyte blastogenesis and migration inhibition factor production following *in vitro* stimulation with nitrofurantoin were demonstrated and found to persist for as long as 2-1/2 years in a patient who had experienced a typical acute reaction to the drug. Although previous investigators also utilized *in vitro* studies to assess cell mediated responsiveness to nitrofurantoin in presumed "sensitive" individuals^{6, 7}, attempts to correlate cell memory with clinical hypersensitivity were inconclusive.

We have not been able to further elucidate the pathogenesis of this syndrome by the present investigation. The *in vitro* response of lymphocytes to nitrofurantoin in our patient clearly showed stimulation when compared with a variety of control subjects and we failed to demonstrate any antinitrofurantoin humoral activity by a very sensitive assay. It should be recognized that the patient may have developed specific antibodies against an unknown metabolite of the drug which were not reactive with the native compound. However, in view of the fact that we, as well as others⁶⁻⁸, have detected immunologic memory cell reactivity against the native compound, it would appear unlikely that failure to detect antibodies can be solely attributed to differences in the chemical form of the test antigen.

* Dr. Charles W. Thompson kindly referred this patient for study.

† Supplied by Eaton Laboratories, Division of the Norwich Pharmacal Company, Norwich, New York.

References

1. WHITCOMB, M. E.: Drug-induced lung disease. *Chest*, 1973, 63, 418.
2. ROSENOW, E. C., III: The spectrum of drug-induced pulmonary disease. *Ann. Int. Med.*, 1972, 77, 977.
3. BRETTNER, A., et al: Pulmonary complications of drug therapy. *Radiology*, 1970, 96, 31.
4. ISRAEL, H. L., et al: Recurrent pulmonary infiltration and pleural effusion due to nitrofurantoin sensitivity. *New Eng. J. Med.*, 1962, 266, 1024.
5. LARSSON, S., et al: Pulmonary reaction to nitrofurantoin. *Scand. J. Resp. Dis.*, 1973, 54, 103.
6. TOSSI, B., et al: Sensibilità alla nitrofurantoina di linfociti umani in cultura. *Arch. Sci. Med.*, 1968, 125, 471.
7. ROCKLIN, R. E., et al: Detection in vitro of cellular hypersensitivity to drugs. *J. All. Clin. Immun.*, 1971, 48, 276.
8. PEARSALL, H. R. et al: Nitrofurantoin lung sensitivity: Report of a case with prolonged nitrofurantoin lymphocyte sensitivity and interaction of nitrofurantoin stimulated lymphocytes with alveolar cells. Presented at AMA Annual Meeting, New York, June 1973.
9. JANICKI, B. W., et al: Tuberculin antigens active in human lymphocyte blastogenesis. *Proc. Soc. Exper. Biol. Med.*, 1972, 141, 809.
10. ROSENOW, E. C., III, et al: Chronic nitrofurantoin pulmonary reaction: Report of five cases. *New Eng. J. Med.*, 1968, 279, 1258.
11. RUIKKA, I., et al: Progressive pulmonary fibrosis during nitrofurantoin therapy: A case history with autopsy report. *Scand. J. Resp. Dis.*, 1971, 52, 162.
12. KOCH-WESER, J., et al: Adverse reactions to sulfisoxazole, sulfamethoxazole, and nitrofurantoin: Manifestations and specific reaction rates during 2,118 courses of therapy. *Arch. Intern. Med.*, 1971, 128, 399.
13. HAILEY, F. J., et al: Pleuropneumonic reactions to nitrofurantoin. *New Eng. J. Med.*, 1969, 281, 1087.
14. MURRAY, M. J., et al: Pulmonary reactions simulating cardiac pulmonary edema caused by nitrofurantoin. *New Eng. J. Med.*, 1965, 273, 1185.
15. MCCOMBS, R. P.: Diseases due to immunologic reactions in the lungs. *New Eng. J. Med.*, 1972, 286, (Part One) 1186, (Part Two) 1245.

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Subjective Response to Therapy in Chronic Obstructive Lung Disease

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Abstract

Patients' evaluation of response to therapy in COPD indicated that they obtain subjective benefit from effective inhalation therapy, oral bronchodilators and intermittent antibiotics and such agents should be provided for them. At times, steroids may be used in addition. The patient's response was conditioned by the natural history of his disease as manifested in lung function, history and physical findings and these, as well as drug therapy determine the degree of improvement which therapy can bring.

Regional Ventilation Perfusion Relationship

Evaluation of specific forms of therapy in chronic obstructive pulmonary disease (COPD) is both difficult and confusing. Objective tests of ventilatory function have been most frequently employed in the acute situation, but as blood gas and distribution studies have been added, more questions have been raised than answered. For example, it was well established objectively that aerosol isoproterenol improved spirometric measurements and decreased dyspnea in patients with COPD, particularly asthmatics^{1,2}. Subsequently, however, it has been demonstrated that this drug often results in decreased arterial oxygenation and deterioration in regional ventilation perfusion despite

decreased airway resistance^{3,4,5,6}. In addition, in some patients it induced severe bronchospasm.⁷ This investigation was designed to study patient assessment of the efficacy of his usual medications, and to analyse its significance in the light of clinical and physiological patterns, and applied pharmacology.

Materials and Methods

The material consisted of 223 subjects with COPD and included both clinic and private patients. The following lung function tests were done in conventional fashion: vital capacity (VC), one second timed vital capacity (FEV_{1.0}), maximum voluntary ventilation (MVV), functional residual capacity (FRC), diffusing capacity (DLCO) and pCO₂ at the end of tidal volume and forced expiration. Total lung capacity (TLC), residual volume (RV), RV/TLC ratio and Δ pCO₂ (forced expiratory pCO₂-end tidal pCO₂) were calculated. The patient's therapy, current and past, was itemized and the patient was asked to characterize his response to each as excellent, good, moderate, slight or none, and to evaluate his overall response to treatment in similar terms. A standardized, quantitative history and physical examination was performed. Particular emphasis was placed upon age at onset, type of onset, and the patient's current symptoms in terms of cough, sputum

production, wheezing, exercise tolerance, and rate of change in exercise tolerance. The physical findings which were carefully quantitated included chest contour, breath sound intensity, and adventitious sounds. The data were transcribed to punch cards and statistical evaluation was performed by standardized methods using an IBM 360 computer.

Results

A. Modalities Used (Table 1) The most commonly employed methods of therapy were inhalation therapy (used in 75%), antibiotics (61%), oral bronchodilators (56%), and expectorants (51%). Compressed gas nebulizer and IPPB/1 were the most frequently currently employed forms of inhalation therapy and hand bulb nebulizers were not often used. Antibiotics were usually used intermittently rather than continuously. The mean number of methods of therapy ever employed was 3.7 per patient and currently employed was 2.7. Thus, multiple therapy was the usual situation.

B. Patient Evaluation of Response (Table 2) Patients who had received therapy rated their overall response as excellent in 22%, good in 23%, moderate in 21%, slight in 16% and none in 18%. Analysis of separate modalities of therapy revealed that some forms were rated as more effective than others. Inhalation of bronchodilator aerosols (whether by hand nebulizer,

compressed gas nebulizer, or by IPPB) and injected bronchodilators scored highest with ratings of good or excellent in 70-79%. Antibiotics used continuously or intermittently were rated good or excellent by 60-69% of subjects. Oral and rectal bronchodilators and steroids were each rated good or excellent in 50-59%. Expectorants, antitussives, antihistamines and allergy desensitization were rated as of decreasing utility.

C. Cessation of Therapy (Table 1) Approximately one-quarter of the therapeutic methods initiated were subsequently stopped. The modalities which were stopped with least frequency were IPPB in 4%, oral bronchodilators in 18%, expectorants in 19%, intermittent antibiotics in 22%, and compressed gas nebulizers in 25%. In considering why patients stopped or continued treatment for each modal-

ity, an analysis was made of the percentage of patients with good or excellent results in those who continued therapy as opposed to those who stopped. (Table 2) Except for oral bronchodilators and intermittent antibiotics, the patients who continued therapy had a greater percentage of good or excellent results than those who stopped.

D. Relation of Response to Lung Function (Table 3) The correlation coefficient (r) was obtained between overall response to therapy and each lung function parameter. The lung function parameter which had the highest correlation with response was the diffusing capacity. VC was significantly related, but the value of r was much lower. The remaining lung function parameters had no significant relation to response. No significant correlation was found between overall

therapeutic result and the acute change in VC or MVV in response to aerosol bronchodilators.

E. Relation of Response to History and Physical (Table 4) Correlation coefficient was obtained between overall response to therapy and elements in the history and physical. There was a negative correlation of response with age at onset; i.e., patients older at onset did not respond as well as those younger at onset. There was a positive correlation with exercise tolerance, and a negative correlation with rate of decline in exercise tolerance over the preceding two and five years. Cough severity was negatively correlated with response and sputum quantity had no relation. The presence of a family history of allergy was positively correlated. Current cigarette smoking was negatively correlated with response.

Of the physical findings, the significant correlations with response to therapy were first, the negative relation to decrease in breath sounds; i.e., the more diminished the breath sounds, the poorer the response, and the second, positive relation to wheezing on forced expiration.

TABLE 1. Modalities of therapy employed are listed in column 1. The number of subjects who employed each modality is listed in column 2, along with the percentage of the total number of subjects, 223. Column 3 indicates the number and percent of patients who currently employed each modality of therapy. The percent of those who discontinued each form of therapy is presented in column 4

(1) Modality of Therapy	(2) Ever Employed		(3) Currently Employed		(4) % Who Discontinued
	n	%	n	%	
Inhalation Therapy	167	75			
Hand Nebulizer	30	13	12	5	60
Compressed gas nebulizer	107	48	81	36	25
IPPB (I)	91	41	87	39	4
Bronchodilators by Non-Inhaled Route					
Oral	125	56	103	46	18
Injected	28	13	15	7	49
Rectal	35	16	18	8	46
Antibiotics	136	61			
Intermittent	127	57	99	44	22
Continuous	13	6	8	3	38
Expectorants	113	51	91	41	19
Steroids	63	28	44	20	32
Antitussives	47	21	28	12	40
Antihistamines	13	6	5	2	62
Desensitization	27	12	9	4	67

Discussion

This study shows that the medications usually employed in COPD have distinctively different degrees of subjective effectiveness. The forms of therapy which were most frequently rated good or excellent proved to be those which were most frequently prescribed and least likely to be discontinued. As each of these was rated independently of the others, it suggests that convenient aerosol bronchodilators, intermittent antibiotics, and oral bronchodilators should be offered to each patient with COPD. Supplementary therapy, such as steroids and expectorants, may be added when there are special indications. Expectorants are the subject of con-

SUBJECTIVE RESPONSE IN CHRONIC LUNG DISEASE

SILVER AND EATON

TABLE 2. This table lists the modalities of therapy in column 1. The percent of patients whose response was good or excellent is shown in column 2. The breakdown of these responders between those who continued and those who stopped therapy is shown in column 3 and 4 respectively

Modality	% Good or Excellent		
	in all subjects	continued therapy	stopped therapy
(1)	(2)	(3)	(4)
Hand nebulizer	73	83	67
Compressed gas nebulizer	78	87	50
IPPB (I)	79	80	50
Oral bronchodilator	52	48	68
Injectable bronchodilator	77	87	69
Rectal bronchodilator	51	61	41
Intermittent antibiotics	66	66	68
Continuous antibiotics	69	88	40
Expectorants	43	44	41
Steroids	55	59	48
Antitussives	32	36	26
Antihistamines	15	20	13
Desensitization	14	22	11

siderable question, based upon studies which have failed to show effectiveness objectively, but there may be some patients who are biologically different from those studied, and there are some physicians in this study who employed larger drug doses than were tested, so the issue is not closed.

Medications are often discontinued by patients and our data offer possible insights. Antihistamines and desensitization were stopped in the highest percentage, and this is believed to represent lack of efficacy as well as the inconvenience and cost of the latter. The other modalities which were discontinued in 40% or more included injected and rectal bronchodilators, which are not convenient for continued use, and hand bulb nebulizers, which are inconvenient and should be replaced by more suitable forms of inhalation therapy. Finally, for almost every method, patients with favorable response were more likely to continue therapy than those with less favorable response. Thus, it appears that continued therapy with any modality depends on its general effectiveness, its effectiveness in the individual patient and convenience of administration. Another factor, undesirable side effects, has not been assessed in this study but must be kept in mind.

Perhaps more important, the overall subjective response to therapy was not a purely chance phenomenon, because each individual's disease pattern played a significant role in determining the outcome of therapy. The high correlation with diffusing capacity is interpreted to mean that the patient with least disruption of vascular bed has the best capability of responding to therapy^{8,9}. The finding that acute response of ventilatory tests to aerosol bronchodilator was not significantly related to overall response re-enforces the position that undue importance should not be ascribed to acute response in the test situation.

TABLE 3. The correlation coefficient (*r*) is listed between overall response to therapy and physiological tests of lung function and response.

(* = $p < .05$; ** = $p < .01$)

Parameter	<i>r</i>
Vital capacity	ml .18*
	% of Pred .17*
Forced Expiratory Volume, 1 sec	% of VC .06
	ml .13
Maximum Voluntary Ventilation	L/min .15
	% of Pred .13
Residual Volume Total Capacity	% .15
pCO ₂ Forced Expiratory	mm Hg .03
ΔpCO ₂ (End-Tidal-Forced Expiratory)	mm Hg .05**
Diffusing Capacity	ml/min/mm .42
Response to Aerosol Bronchodilators	Δ VC % of Pred -.03
	Δ MVV % of Pred -.05

The significant relationship of response to elements in the history is also of interest. Early age at onset and positive family history of allergy identify patients with primarily airway disease, hence responsiveness. On the other hand, those with late onset and greatest rate of decline in exercise tolerance during the preceding two and five years are most likely those with parenchymal disruption and therefore those are least likely to respond to any therapy.

The finding that decreased breath sounds were related to poor response, and that the degree of wheezing on forced expiration was associated with good response, may be explained by regarding the former as indicative of parenchymal destructive disease and the latter of reversible airway disorder and by considering that the relationship of the physical findings to subjective response is also soundly based in the patient's disease pattern.

With respect to evaluation of therapy in COPD, it is suggested that the acute objective study, no matter how elegant, is subject to question

concerning its relevance to long term utility. All too often the subjects chosen for a pharmacological study are either deliberately or subconsciously selected because they are thought to have a large bronchospastic element and are often the younger, more allergic patients. Unless the characteristics of each individual are carefully described, the relevance of the investigation to the general population of COPD patients is undeterminable. In addition, drug interaction, enzyme induction and cumulative effects may alter response, and this is not usually evaluated in the acute study protocol¹⁰

Patient evaluation of therapy, however unscientific it may appear at first glance, relates pharmacological actions with the natural history of COPD and provides insights into interactions which help in understanding and treating patients with this long-term illness in which several forms of concurrent therapy are employed.

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References

1. LOWELL, F. C., CURRY, J. J., SCHILLER, I. W.: A clinical and experimental study of isuprel in spontaneous and induced asthma, *New Eng. J. Med.*, 1949, 240, 45.
2. KNUDSON, R. J., CONSTANTINE, H. P.: An effect of isoproterenol on ventilation-perfusion in asthmatic versus normal subjects, *J. Appl. Physiol.*, 1967, 22, 402.
3. PALMER, K. N. V., DIAMENT, M. L.: Effect of aerosol isoprenaline on blood-gas tensions in severe bronchial asthma, *Lancet*, 1967, 2, 1232.
4. INGRAM, R. H., KRUMPKE, P. E., DUFFELL, G. M., MANISCALO, B.: Ventilation-perfusion changes after aerosolized isoproterenol in asthma, *Am. Rev. Resp. Dis.*, 1970, 101, 364.

5. GAZIOGLU, K., CONDEMI, J. J., HYDE, R. W., KALTREIDER, N. L.: Effect of isoproterenol on gas exchange during air and oxygen breathing in patients with asthma, *Am. J. Med.*, 1971, 50, 185.
6. WATANABE, S., RENZETTI, A. D. JR., BIGLER, A.: Bronchodilator and corticosteroid effects on regional and total airway resistance in patients with asthma, chronic bronchitis, and chronic pulmonary emphysema, *Am. Rev. Resp. Dis.*, 1972, 106, 392.
7. KEIGHLEY, J. F.: Iatrogenic asthma associated with adrenergic aerosols, *Ann. Int. Med.*, 1966, 65, 985.
8. OGILVIE, C.: Patterns of disturbed lung function in patients with chronic obstructive emphysema, *Thorax*, 1959, 14, 113.
9. ZISKIND, M.: Chronic bronchitis? Pulmonary emphysema? *Arch. Int. Med.*, 1961, 108, 335.
10. BASS, H.: Endogenous regulation of the pulmonary response to isoproterenol, *Chest*, 1972, 61, 14.

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TABLE 4. The correlation coefficient (*r*) is listed between overall response to therapy and various elements of history and physical.

Parameter	<i>r</i>
Age at onset of dyspnea	-.22**
Level exercise tolerance	.18*
Step exercise tolerance	.26**
Exercise tolerance 2 years	-.28**
Exercise tolerance 5 years	-.29**
Cough Severity	-.18*
Sputum quantity	-.03
Allergy Index	.18*
Current cigarette consumption	-.20*
Cyanosis	-.02
Clubbing	-.02
PA chest diameter	-.01
Breath sounds decreased	-.18*
Expiratory wheeze	.13
Forced expiratory wheeze	.16*
Rales, crepitant	-.07

Busulfan Lung Complicated by *Pneumocystis carinii* and Cytomegalovirus Infection

GERALD I. GREEN, M.D., RICHARD L. LEVIN, M.D., LAWRENCE E. PIERCE, M.D. AND PHILIP WITORSCH, M.D.

Abstract

A patient with chronic myelogenous leukemia undergoing therapy with busulfan developed progressive shortness of breath and a diffuse pulmonary infiltrate. Percutaneous lung biopsy revealed pulmonary fibrosis and, in addition, typical findings of cytomegalovirus infection. Busulfan was discontinued and treatment was instituted with prednisone and cytosine arabinoside. In spite of this therapy the patient died of progressive pulmonary insufficiency. Postmortem examination revealed a significant increase in the degree of pulmonary fibrosis and the additional complication of *Pneumocystis carinii* infection of the lungs, but no evidence of residual cytomegalovirus in the lungs. The relatively unusual association of these three entities and the possible efficacy of cytosine arabinoside therapy for cytomegalovirus infection are discussed.

Introduction

Busulfan (1,4-dimethanesulfonylbutane) (Myleran) is widely used for the treatment of chronic myelogenous leukemia and when effectively administered, induces remissions in the majority of patients for prolonged periods of time¹.

The most frequent toxic side effect of busulfan is myelotoxicity, which is

usually dose related, but may rarely occur with small doses of the drug². A relatively common side effect is hyperpigmentation of the skin, usually observed in patients who have been on therapy for two or more years³. Less frequently, an Addisonian-like syndrome has occurred in a few patients⁴. In 1961, Oliner et al.⁵ reported the first recognized cases of pulmonary fibrosis associated with busulfan therapy, but fewer than twenty additional documented cases have been reported since their original description⁶. Although one of the most serious side effects, it is possible that proper therapy may be instituted in time to prevent irreversible lung damage.

The present report describes a patient who developed severe busulfan induced pulmonary fibrosis, and who, in addition, simultaneously acquired pulmonary infection due to *Pneumocystis carinii* and cytomegalovirus.

Case Report

D. W., a 52-year-old negro housewife, was hospitalized on July 18, 1970, because of progressive weakness and shortness of breath. In January of 1966, she noted the onset of spontaneous purpura and epistaxis, and was found to have hepatosplenomegaly and a total white blood cell count of 180,000/mm³. A diagnosis of chronic myelogenous leukemia was established and therapy was initiated with busul-

fan at a dose of 6 mg daily. She was followed as an outpatient, with periodic regulation of the busulfan dosage at between 2 and 4 mg per day to control the disease.

The patient did well until April of 1970, when she began to note malaise, fatigue and mild cough productive of small amounts of yellow sputum. Chest x-ray was normal and sputum culture grew normal flora. Splenic size increased; the platelet count rose to 1.6 million per mm³ and there were increased numbers of nucleated red blood cells in the peripheral smear. The patient was begun on erythromycin, 250 mg four times per day for a total of 10 days. Cough and sputum production persisted, and shortness of breath developed. When seen in June of 1970 she was noted to have sustained a 25 lb. weight loss. Physical examination at that time revealed coarse bibasilar rales and rhonchi, but she remained afebrile and the chest x-ray was again normal. Multiple repeated sputum cultures (routine, fungal and acid-fast) revealed no pathogens. Due to the persistence and progression of the patient's symptoms, she was hospitalized on July 18, 1970.

Physical examination revealed a poorly nourished, alert, tachypneic, slightly cyanotic woman, appearing chronically ill but in no acute distress. Blood pressure was 122/70 mm Hg, pulse 92 per minute and regular, respirations were shallow at 30 per

minute, and temperature 99F orally. The skin, particularly over the palms and elbows, and the oral mucosa were hyperpigmented. Examination of the lungs revealed diffuse bilateral rales, most marked in the basal area. A firm, non-tender spleen descended 6 cm below the left costal margin, and the liver could not be palpated. There was no clubbing, and the remainder of the physical examination was unremarkable.

Pertinent laboratory data included: hemoglobin 11.5 g/100 ml; hematocrit 38%; white blood count 10,400 per mm^3 with 48% neutrophils, 25% bands, 15% metamyelocytes, 12% myelocytes and 28 nucleated red blood cells per hundred white cells; platelet count 1,050,000 per mm^3 ; serum albumin 2.3 g/100 ml; serum globulins 3.4 g/100 ml; serum glutamic pyruvic and oxaloacetic acid transaminases 44 and 67 International Enzyme units respectively; serum lactic dehydrogenase 660 International Enzyme units; serum alkaline phosphatase 24.5 Bessey-Lowry units, with 68% heat stable. Arterial PO_2 was 32 mm Hg, PCO_2 37 mm Hg, and pH 7.48. Chest x-ray revealed a bilateral, diffuse linear-reticular parenchymal infiltrate, compatible with an interstitial process (Figure 1). Additional normal laboratory studies included blood urea nitrogen, glucose, serum creatinine, electrolytes, urinalysis, plasma cortisol, urinary corticosteroids, and total basophil count. Initial sputum culture grew normal flora and a few *Candida* species.

The patient was placed on oxygen by nasal cannula at a flow rate of four to five liters per minute, with a resultant rise in arterial PO_2 to 52 mm Hg. Arterial PCO_2 rose to 46 mm Hg and pH fell to 7.40. Arterial blood gases remained at approximately these levels for the remainder of her hospital course. Busulfan was discontinued and the patient was given 1 millicurie of P^{32} intravenously (primarily because



FIG. 1. Chest x-ray of July 18, 1970, showing a diffuse, linear-reticular parenchymal infiltrate, compatible with an interstitial process.

of the level of thrombocytosis). Repeat sputum culture obtained on the second hospital day grew *E. coli* and *Klebsiella-Enterobacter*, and therapy was begun with parenteral administration of ampicillin and kanamycin. This eradicated these organisms from the sputum, but there was no change in the chest x-ray or clinical picture. Consequently, on the 9th hospital day a percutaneous needle biopsy of the right lung was performed. The procedure was well tolerated, except for a 15% pneumothorax which quickly resolved.

Histologic examination of the biopsy specimen revealed diffuse interstitial fibrosis, with minimal inflammatory infiltrate. The alveolar spaces were lined by cells which were markedly enlarged and contained typical intranuclear inclusions of cytomegalovirus, with associated basophilic cytoplasmic granules (Figures 2, 3). The alveoli were mainly empty, but occasional alveolar spaces contained fibrinous exudate. Gomori methenamine silver stains revealed no definite organisms within the alveolar spaces.

It was assumed that the patient had pulmonary fibrosis secondary to busulfan, and in addition, cytomegalovirus infection. She was placed on 80 mg of prednisone daily for the former, and

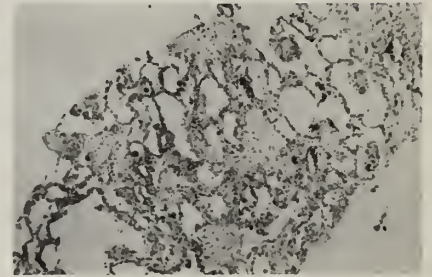


FIG. 2. Needle biopsy specimen of the lung showing diffuse interstitial fibrosis with minimal inflammatory infiltrate. Alveolar spaces are lined by cells containing intranuclear inclusions. (Hematoxylin and eosin; original magnification $\times 35$.)

although the clinical significance of the cytomegalovirus infection was uncertain, the risk of disseminating this infection with steroid therapy was deemed sufficient to justify treatment with cytosine arabinoside. Therefore, cytosine arabinoside, 2 mg/kg body weight per day intravenously (daily doses of 120 mg given over a 24 hour period) for five days, was also administered. Prednisone was continued until the 19th hospital day, at which time, because of the development of confusion and disorientation thought to represent steroid psychosis, the dose was lowered to 30 mg per day and continued for the remainder of the

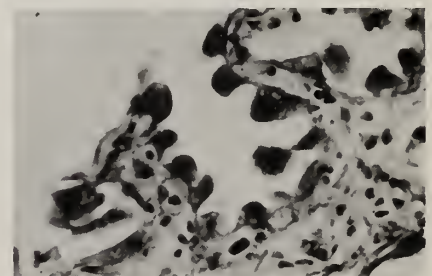


FIG. 3. Higher magnification of Figure 3 showing the typical intranuclear inclusions surrounded by a halo. The cytoplasm contains associated basophilic granules. (Giemsa; original magnification $\times 450$.)

BUSULFAN LUNG WITH PNEUMOCYSTIS AND CYTOMEGALOVIRUS

GREEN, LEVIN, PIERCE AND WITORSCH

patient's hospital course. In spite of this therapy, the chest x-ray progressively worsened (Figure 4), as did the patient's clinical picture, and she expired on the 30th hospital day.

A serum specimen which had been obtained prior to the institution of cytosine arabinoside therapy was tested for complement-fixing antibodies to cytomegalovirus and revealed a titer of 1:8. Urine, sputum and salivary specimens that had been obtained prior to therapy for viral culture were contaminated by bacterial overgrowth.

At autopsy, the lung parenchyma was found to be diffusely replaced by firm yellowish-white tissue concentrated in the central portions. The lungs had a combined weight of 1400 g. There were petechial hemorrhages over the visceral pleura, and the cut surfaces of the lung exuded edema fluid. Microscopic examination revealed extensive interstitial fibrosis, with chronic inflammation of alveolar septae. The alveoli contained hemorrhagic, fibrinous exudate and exfoliated macrophages. There was intra-alveolar organization of this exudate with connection to the fibrotic septae. Large, pleomorphic and hyperchromatic cells lined the alveolar spaces and bronchial walls, but the nuclei were homogenous and contained no inclusions. Clusters of *Pneumocystis carinii* were found in the alveoli stained with Gomori methenamine silver (Figure 5).

Similar dysplastic epithelial cells were also found in the pancreatic acini, renal tubules, adrenal cortex, and urinary bladder. In addition, there was an area of necrosis in one adrenal cortex which contained typical cytomegalovirus-type inclusions (Figure 6).

The spleen and liver were moderately enlarged, with focal areas of leukemic infiltrate and extramedullary hematopoiesis. Multiple sections of

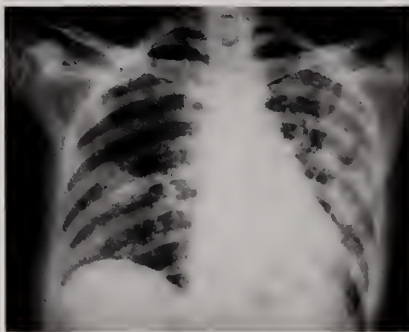


FIG. 4. Chest x-ray on the 26th hospital day showing further progression of the parenchymal infiltrate.

bone marrow revealed hypocellularity of medullary elements.

Discussion

Busulfan is an alkylating agent which has "radiomimetic" properties, and the mechanism of its production of pulmonary fibrosis may be analogous to that occurring following pulmonary irradiation. Similarly, diffuse pulmonary fibrosis has been described in hypertensive patients treated with hexamethonium⁷, a drug somewhat similar in chemical structure to busulfan. Recently, pulmonary fibrosis has been reported to occur in some patients with chronic myelogenous leukemia who have not received busul-

fan⁸, although the degree of involvement appears to be less than that among patients treated with the drug.

In an original description of pulmonary fibrosis secondary to busulfan, Oliner et al.⁵ considered hypersensitivity to be a likely etiologic mechanism and, in fact, demonstrated pulmonary vasculitis in one case. This observation has not been confirmed in subsequent reports⁶. Two of their patients responded to steroid therapy with improvement in their clinical and radiographic status. It appears that those patients responsive to steroids do so only when large doses (50-100 mg of prednisone per day) have been administered⁵. Our patient received large doses of prednisone (80 mg per day), but a considerable period of time had elapsed between the onset of symptoms and the initiation of therapy. This situation is similar to that encountered by Littler et al.⁶, who felt that improvement with steroids tended to occur only if they were administered during the early stages of the disease process, and that once significant fibrosis had developed, there was little hope of arresting or improving the condition.

Although a lung biopsy was considered to be hazardous in this patient, it was felt necessary in order to establish a diagnosis, of which the prime consid-

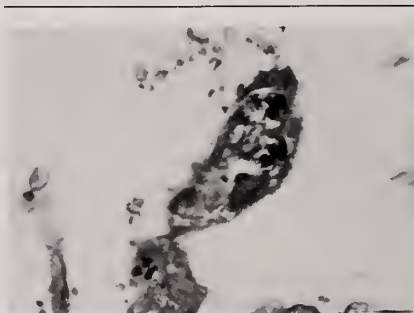


FIG. 5. Clusters of *Pneumocystis carinii* in the alveolar spaces. (Gomori methenamine silver; original magnification $\times 450$.)

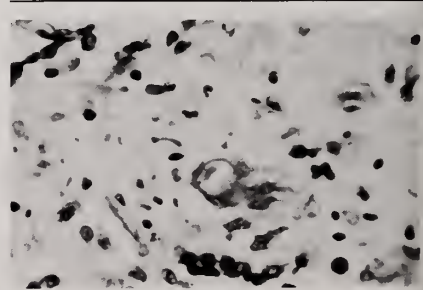


FIG. 6. Adrenal cortex showing an area of necrosis containing typical cytomegalovirus inclusion bodies. (Giemsa; original magnification $\times 450$.)

erations were: 1) busulfan-induced pulmonary fibrosis; 2) *Pneumocystis carinii* or other infections; 3) leukemic pulmonary infiltration. The biopsy specimen was stained with Gomori methenamine silver in hopes of finding *Pneumocystis*, however, the organism was not identified except in retrospect, when a few cysts were seen in a small corner of the section. This emphasizes the limitations inherent in needle biopsy of the lung, where a relatively small and possibly unrepresentative sample may be obtained, and also illustrates the inhomogeneity of involvement as well as the need for careful, meticulous examination of appropriately stained specimens.

The postmortem microscopic examination of our patient's lungs revealed a significant increase in the degree of pulmonary fibrosis as compared to the antemortem biopsy specimen. This may have been because the area biopsied was not truly representative, or because the disease had progressed. Recently, Whitcomb et al.⁹ described the occurrence of pulmonary fibrosis in a patient with *Pneumocystis pneumonia* who was treated with pentamidine isethionate. In that case, the initial lung biopsy did not show fibrosis, while a second biopsy obtained five months later revealed significant interstitial fibrosis. Although a definite cause and effect relationship between fibrosis and *Pneumocystis* remains to be established, one may consider a possible association between the infection and the apparent progression of fibrosis.

Pneumocystis pneumonia has usually been recognized in the debilitated newborn infant, in individuals with a variety of immunologic deficiencies, in renal transplant recipients receiving immunosuppressive and corticosteroid therapy and in patients with leukemia or lymphoma under treatment with corticosteroids and/or cytotoxic agents^{10,11}. Although chronic

myelogenous leukemia and busulfan therapy have been described as predisposing factors to the development of *Pneumocystis pneumonia*, they are relatively uncommon when compared to other known causes^{10,11}.

Cytomegalovirus infection is common in the general population, but its precise clinical significance is uncertain. Overt clinical disease in the adult has been uncommon, but renewed interest has resulted from the recognition of this infection in patients receiving renal transplants¹². Pulmonary and disseminated cytomegalovirus infection has been documented to occur in adults with leukemia, lymphoproliferative disorders and other conditions in which cytotoxic therapy is given, and has been implicated as a cause of death in some instances¹³. Significantly, cytomegalovirus has commonly been found in association with *Pneumocystis carinii* infection of the lung¹⁴. A patient has been reported with chronic myelogenous leukemia treated with busulfan (duration of therapy not specified), who at autopsy was found to have interstitial pulmonary fibrosis, pulmonary cytomegalic inclusion disease, and *Pneumocystis pneumonia*¹⁵. This association of these three entities is unusual, and is identical to that observed in our patient.

Cytomegalovirus complement-fixing antibody has been found in 51 to 81 per cent of adults over the age of 35¹⁶, the majority of whom have no clinical or radiographic evidence of infection. Thus, the presence of a positive titer is evidence only of prior exposure to the virus, and a rising titer does not necessarily imply clinically significant infection. Conversely, a negative titer does not exclude significant infection¹⁷. We could not, therefore, make a judgment regarding therapy based solely upon our patient's complement-fixation titer of 1:8, but in view of the presence of histologic

evidence of infection in the biopsy specimen, and the risk of disseminating the infection with steroids, it was felt justified to administer specific therapy directed against cytomegalovirus.

At present, specific therapy for cytomegalovirus infection is limited. Gamma globulin has been used, but in general without remarkable benefit¹⁸. Floxuridine has been used to treat cytomegalovirus pneumonia complicating acute leukemia with good results¹⁸, and idoxuridine has been used with some success in the treatment of congenital cytomegalovirus infection¹⁹.

Cytosine arabinoside has not heretofore been used in the treatment of cytomegalovirus infection. It is a pyrimidine nucleoside analogue that inhibits DNA synthesis, and has been used predominantly for the treatment of acute leukemia²⁰. It inhibits both Herpes zoster and Herpes simplex viruses in vitro, and has been used topically to treat herpetic keratitis²¹. The drug has also been used successfully to treat fulminant varicella and disseminated zoster²². It is of interest that no evidence of cytomegalovirus was found in our patient's postmortem lung specimen, although there was evidence of residual infection in the adrenal gland. We can only speculate that the drug may have eradicated the organism from the pulmonary tissue, and suggest that further studies with this agent in cytomegalovirus infection may be warranted.

Undoubtedly, the pulmonary fibrosis was the major factor contributing to this patient's deteriorating pulmonary picture and ultimate demise. The additional complications of *Pneumocystis carinii* and cytomegalovirus infection were interesting and complicating facets. The possibility of specific modes of therapy for all three entities may make the outlook for patients with these problems less ominous.

BUSULFAN LUNG WITH PNEUMOCYSTIS AND CYTOMEGALOVIRUS

GREEN, LEVIN, PIERCE AND WITORSCH

Acknowledgements

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References

- HAUT A., ALTMAN S. J., CARTWRIGHT G. W. et al: The use of Myleran in the treatment of chronic myelocytic leukemia. *Arch Intern Med* 96, 1955, 451-462.
- GALTON D. A. G., TILL M., WILTSHAW E.: Busulfan (1,4-dimethanesulfonyloxybutane, Myleran): Summary of clinical results. *Ann N.Y. Acad Sci* 68, 1958, 967-973.
- HAUT A., ABBOTT W. S., WINTROBE M. M. et al: Busulfan in the treatment of chronic myelocytic leukemia. The effect of long term intermittent therapy. *Blood* 17, 1961, 1-19.
- HARROLD B. P.: Syndrome resembling Addison's disease following prolonged treatment with busulfan. *Brit Med J* 1, 1966, 462-464.
- OLINER H., SCHWARTZ R., RUBIO F. et al: Interstitial pulmonary fibrosis following busulfan therapy. *Amer J Med* 31, 1961, 134-139.
- LITTLER W. A., KAY J. M., HASLETON P. S. et al: Busulfan lung. *Thorax* 24, 1969, 639-655.
- PETERSEN A. G., DODGE M., HELWIG E. C.: Pulmonary changes associated with hexamethonium therapy. *Arch Intern Med* 103, 1959, 285-288.
- KIRSCHNER R. H., ESTERLY J. R.: Pulmonary lesions associated with busulfan therapy of chronic myelogenous leukemia. *Cancer* 27, 1971, 1074-1080.
- WHITCOMB M. E., SCHWARZ M. I., CHARLES M. A.: Interstitial fibrosis after *Pneumocystis carinii* pneumonia. *Ann Intern Med* 73, 1970, 761-765.
- VOGEL C. L., COHEN M. H., POWELL R. D. et al: *Pneumocystis carinii* pneumonia. *Ann Intern Med* 68, 1968, 97-108.
- GOODELL B., JACOBS J. B., POWELL R. D. et al: *Pneumocystis carinii*: The spectrum of diffuse interstitial pneumonia in patients with neoplastic diseases. *Ann Intern Med* 72, 1970, 337-340.
- RIFKIND D., GOODMAN N., HILL R. B., JR.: The clinical significance of cytomegalovirus infection in renal transplant recipients. *Ann Intern Med* 66, 1967, 1116-1128.
- WONG T. W., WARNER N. E.: Cytomegalic inclusion disease in adults. Report of 14 cases with review of the literature. *Arch Path (Chicago)* 74, 1962, 403-422.
- SYMMERS W. ST C.: Generalized cytomegalic inclusion-body disease associated with *Pneumocystis pneumonia* in adults. A report of three cases, with Wegener's granulomatosis, thrombotic purpura, and Hodgkin's disease as predisposing conditions. *J Clin Path* 13, 1960, 1-21.
- CAPERS T. H., LEE D.: Pulmonary cytomegalic inclusion disease in an adult. *Amer J Clin Path* 33, 1960, 238-242.
- STERN H., ELEK S. D.: The incidence of infection with cytomegalovirus in a normal population. A serological study in Greater London. *J Hyg (Camb)* 63, 1965, 79-87.
- DUVALL C. P., CASAZZA A. R., GRIMLEY P. M. et al: Recovery of cytomegalovirus from adults with neoplastic disease. *Ann Intern Med* 64, 1966, 531-541.
- CANGIR A., SULLIVAN M. P., SUTOW W. W., et al: Cytomegalovirus syndromes in children with acute leukemia. *JAMA* 201, 1967, 612-615.
- CONCHIE A. F., BARTON B. W., TOBIN J. O'H.: Congenital cytomegalovirus infection treated with idoxuridine. *Brit Med J* 4, 1968, 162-163.
- ELLISON R. R., HOLLAND J. F., WEIL M. et al: Arabinosylcytosine: A useful agent in the treatment of acute leukemia in adults. *Blood* 32, 1968, 507-523.
- KAUFMAN H. E., MALONEY E. D.: IDU and cytosine arabinoside in experimental herpetic keratitis. *Arch Ophthal* 69, 1963, 626-629.
- CHOW A. W. C., FOERSTER J., HRYNIUK W.: Cytosine arabinoside therapy for Herpes virus infections. *Antimicrobial Agents and Chemotherapy*. 1970, 1971, 214-217.
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The Definitive Diagnosis and Treatment of Pulmonary Disease By Selective Bronchial Catheterization

S. DAVID ROCKOFF, M.D.

Introduction

Selective bronchial catheterization has been used in over 500 patients in order to accomplish the following in the lung:

- 1) To diagnose malignant disease
- 2) To diagnose inflammatory disease
- 3) To treat lung abscesses
- 4) To diagnose bronchial disorders definitively

The application of this method which has often precluded surgery is illustrated in this report. All complications have been minor, consisting of subcutaneous emphysema in approximately one-third of patients, occasional mediastinal emphysema, two instances of pneumothorax and two of gross hemoptysis.

The most common course of action in the management of a patient with a pulmonary lesion on chest radiography, for which no reliable criteria of benignancy are present (i.e., large, dense central or ring like calcifications), and from whom no definitively diagnostic material can be obtained non-invasively (i.e., from the sputum), is to resort to a surgical procedure for diagnosis and, possibly, for treatment of the lesion. The surgical approaches to diagnosis may be as simple as bronchoscopy or mediastinoscopy or

may include thoracotomy with removal of all or part of the lung lesion.

The purpose of this report is to describe a relatively non-traumatic approach to the definitive diagnosis of a pulmonary lesion, which may obviate the need for surgical intervention by proving that the lesion is inflammatory rather than malignant or by showing that it is a cancer of a cell type which is not treated well by surgery (i.e., oat cell carcinoma). In addition, the method permits the drainage of inflammatory abscesses which are not communicating with a bronchus, which then can result in healing without surgical intervention. These diagnostic and therapeutic approaches are made possible by the selective catheterization of the bronchial tree.

Following the technique of bronchial catheterization popularized by Fennessy^{1,2}, modified to utilize the transcricothyroid approach³, personal experience with the application of the method to over 500 patients over the past six years forms the basis for this communication to illustrate its uses. These uses can be classified as follows:

- I. Application to the Diagnosis of Malignant Disorders of the Lung.
- II. Application to the Diagnosis of Inflammatory Lesions of the Lung.

III. Application to the Treatment of Lung Abscesses

IV. Application to the Definitive Diagnosis of Bronchial Abnormalities.

Methods

Selective bronchial catheterization is performed as follows:

1. The patient is visited by a radiologist the day prior to the examination, at which time the procedure and its risks are explained to the patient, an informed consent is obtained and the following orders are written, subject to modification depending upon the condition, age and weight of the patient: a. Nothing by mouth after midnight, b. Atropine sulfate 0.6 mg. I.M. on call to x-ray, c. Valium 15 mg I.M. on call to x-ray, d. Male patients are to shave the neck the morning of the examination.

2. At the time of the examination, the anterior portion of the neck, to the base of the mouth and to the level of the clavicles, is prepared with phisohex and betadine. The body is draped to the neck with sterile towels and drapes.

3. A limit of 20 cc of 1% xylocaine is placed on the amount of local anesthetic to be used during the examination, in an attempt to avoid toxicity problems. This is particularly

DIAGNOSIS BY SELECTIVE BRONCHIAL CATHETERIZATION

ROCKOFF

important because of the very rapid absorption of xylocaine from the bronchial mucosa. The skin over the cricothyroid membrane is anesthetized with 1% xylocaine and a small (2 mm) incision is made in the skin. One cc of anesthetic is placed directly into the trachea through the needle used for the skin injection.

4. A curved cricothyroid needle (Cook Co., Bloomington, Indiana #BN-16--50) is inserted through the skin incision, through the cricothyroid membrane and into the trachea. A number 6 guide wire (Cook Co., #SF-35-125) is placed through the needle into the trachea, the point of which is directed toward the carina. The needle is removed over the guide wire while holding it in place with its end about 5 cm into the anesthetized trachea. A radiopaque yellow catheter (Cook Co., 6.7 Fr. 40 cm long) is then placed over the guide wire, inserted into the trachea, and the guide wire is removed. The catheter is often pre-shaped in sterile hot water to permit easier manipulation into the more acutely angled bronchi (i.e. upper lobes and superior segments).

5. Under image intensified fluoroscopic control, the catheter is then advanced into the desired main stem bronchus. A slight curve on the end of the catheter permits directing the tip of the catheter by means of a pill-rolling action on the catheter with the thumb and forefinger at the cricothyroid membrane. If the catheter catches on the tracheal or bronchial mucosa, as often happens when it is pre-curved with a sharp angle, straightening the end of the catheter by inserting the stiff end of the guide wire will permit the catheter to be advanced. From the main stem bronchus, the desired lobar, segmental and subsegmental bronchi can then be entered. Selective placement of the catheter and brush can often be aided by use of special controllable guide

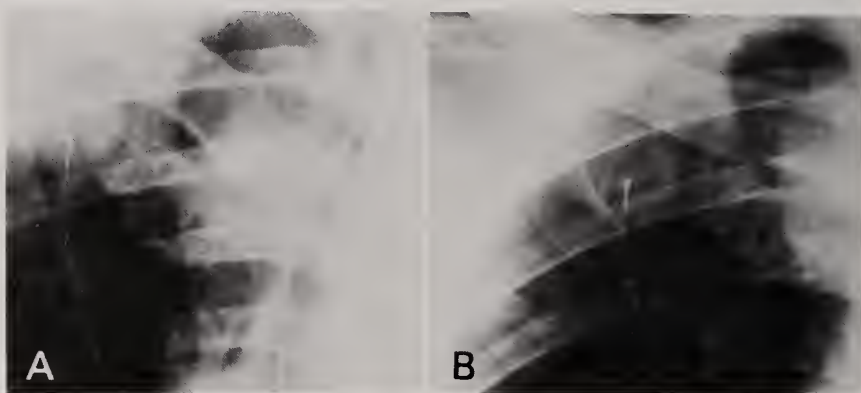


FIG. 1. Selective brush biopsy of right apical nodule with central calcification, diagnosed as adenocarcinoma, demonstrating precision with which biopsy brush can be placed.

wire and brush (Wilson-Eskridge Brushing System, U.S.C.I., Glen Falls, New York 12801). Bronchial aspirations, brushings with a nylon brush and bronchial washings can then be obtained and the material can be sent for cytological and bacteriological study. Contrast material is then injected selectively as is needed.

Results and Discussion

1. Application to the Diagnosis of Malignant Disorders of the Lung

The placement of a selective catheter into a pulmonary carcinoma permits the diagnosis of this lesion without surgery. This is demonstrated in the following examples.

In Figure 1 is shown a patient with a nodule in the right upper lobe. This was selectively catheterized and a brush biopsy was obtained which revealed "malignant cells, probably adenocarcinoma." At surgery, this was proved to be an *adenocarcinoma*.

This case brings out two points. First, extremely accurate peripheral placement of the brush and catheter is

possible and, secondly, carcinomas of the lung can have x-ray demonstrable calcium within them.

In Figure 2 is shown a patient with a cavitary lesion of the right upper lobe, with placement of the biopsy brush into the wall and cavity of the lesion. In Figure 3, a selective bronchogram shows filling of the cavitary lesion with contrast material. Cytologic examination demonstrated carcinoma cells, shown to be from a *squamous cell carcinoma* at surgery. This case demonstrates the very small size of the bronchus which can be successfully catheterized by this method.

We have found this method of diagnosis to be especially valuable in the following situations of carcinoma of the lung:

a. In patients whose physical condition, severe obstructive lung disease or clinical findings (recurrent laryngeal nerve involvement, pulmonary artery invasion, multiple lesions) make them poor candidates for surgery.

b. In situations where an *oat cell carcinoma* may be present, where a proven diagnosis is generally accepted

as indicating an inoperable lesion.

Failure to enter a carcinoma selectively or a *false negative* brush biopsy runs approximately 30%. We have had one *false positive*, in which the specimen from a brush biopsy of a bronchial adenoma was interpreted as a cancer⁴.

II. Application to the Diagnosis of Inflammatory Lesions of the Lungs

Selective bronchial catheterization permits obtaining organisms which are not in free contact with the outside and which cannot be diagnosed in any other non-operative way. Examples of this application include the following:

In Figure 4 is shown the chest of a young woman who had lymphoma which had been treated for a long period of time with immunosuppressive therapy and who had developed a febrile illness and a right upper lobe infiltrate. Selective brush biopsy of the right upper lobe revealed pneumocystis carinii organisms. In Figure 5 is shown improvement after appropriate therapy was given.

In Figure 6A is shown a selective catheter and brush in a left lingular cavity in a young man with a febrile illness in whom no diagnosis could be obtained, including using bronchoscopy. Figure 6B shows a selective bronchogram of the same lesion. Smears and cultures demonstrated tuberculosis organisms.

These two cases demonstrate the definitive diagnosis of pulmonary inflammatory lesions which could be diagnosed in no other way and for which appropriate treatment could then be given.

III. Application to the Treatment of Lung Abscesses

In addition to the diagnosis of the type of infection present, this method

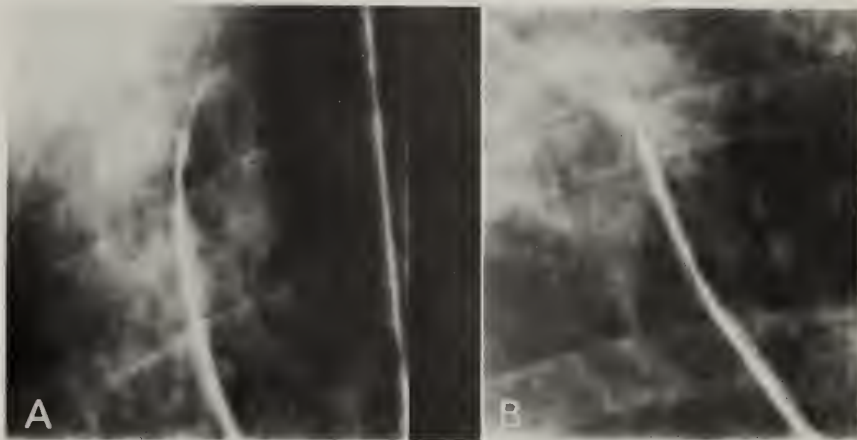


FIG. 2. Selective catheterization and brushing of wall and cavity of cavitory lesion of right upper lobe, diagnosed as squamous cell carcinoma.



FIG. 3. Selective bronchogram of lesion shown in Figure 2, demonstrating cavitory nature of lesion and small size of bronchus which was catheterized to obtain specimen.

DIAGNOSIS BY SELECTIVE BRONCHIAL CATHETERIZATION

ROCKOFF



FIG. 5. Clearing of right upper lobe lesion shown in Figure 4 after treatment, with small residual cystic area.



FIG. 4. Previously undiagnosed right upper lobe infiltrate in patient with lymphoma on long term immunosuppressive therapy. Lesion was diagnosed as due to pneumocystis carinii by material obtained from selective bronchial brushing.

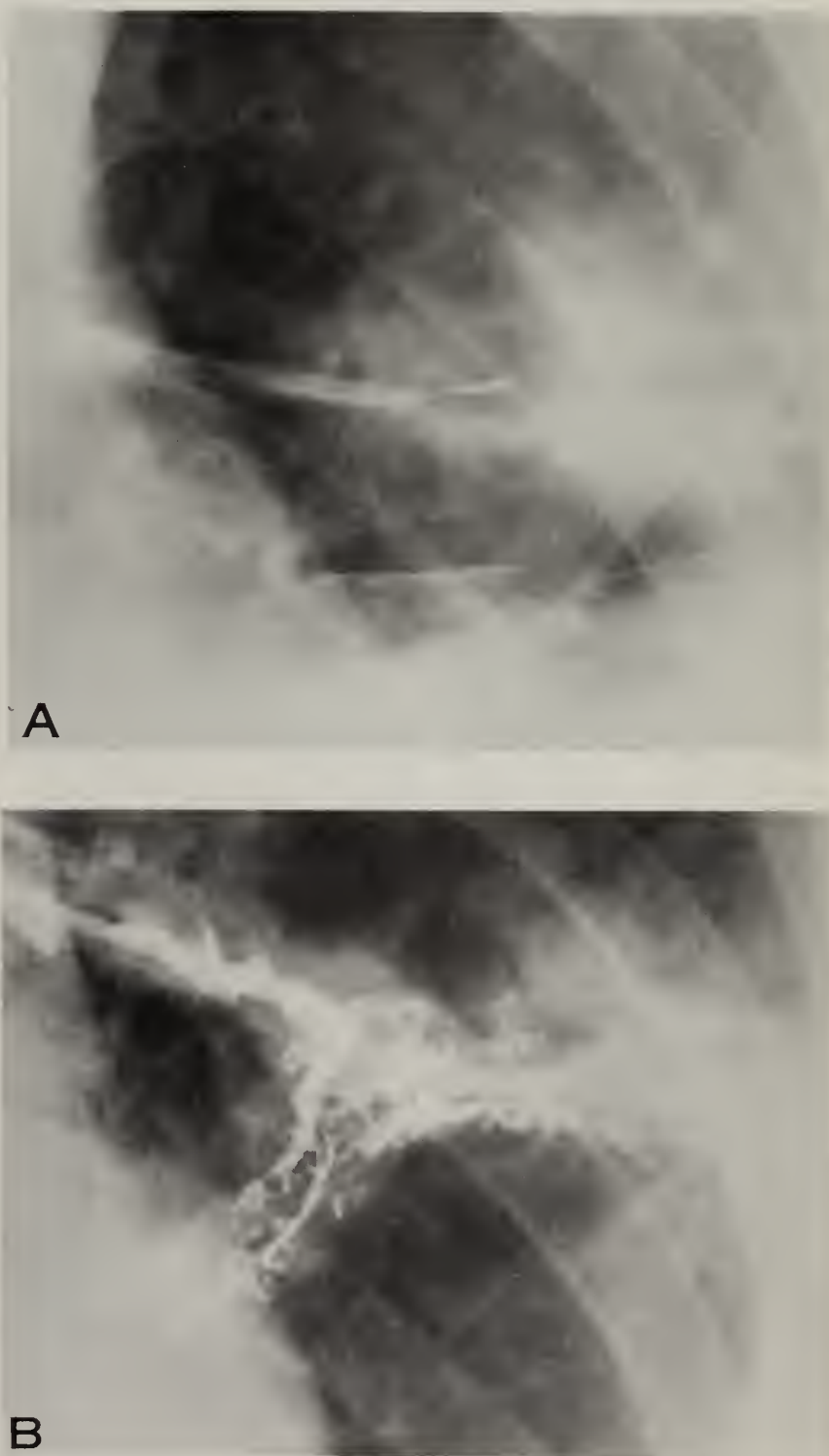
may be of great use in the non-operative treatment of peripheral abscesses which are not responding to treatment. The treatment is achieved by breaking selectively into the cavity, evacuating its contents, and permitting it to drain to the outside via the bronchial tree. Also, the material obtained can be cultured and tested for sensitivity so that the proper antibiotic can be utilized. An example of this application is as follows:

In a young female (Figure 7) an abscess of the superior segment of the left lower lobe had been present for two weeks and was getting worse. In Figure 8 is shown selective catheterization of the lesion from which 30 cc of purulent fluid was obtained. Smears and cultures showed staphylococcus aureus (coagulase positive). After the procedure, the cavity continued to drain freely and with antibiotic therapy complete healing occurred.

IV. Application to the Definitive Diagnosis of Bronchial Abnormalities

Non-selective or semi-selective bronchography is often not definitive because of incomplete filling of the bronchial tree. Selective bronchial

FIG. 6. Selective bronchial catheter and brush in left lingular cavity (A) and subsequent bronchogram (B). Study of material obtained from catheterization showed lesion to be due to tuberculosis.



catheterization permits excellent filling of the bronchi in question, clarifying the situation and preventing other needless tests or surgery. An example of this is as follows:

In Figure 9A is shown a semiselective left bronchogram in a 45 year old male heavy smoker who complained of gross hemoptysis. All semiselective efforts to fill the apical-posterior segment of the left upper lobe failed. Selective catheterization of this bronchus showed it to be normal (Figure 9B). Given the history and failure of bronchial filling, surgery might well have been performed. This was obviated by the selective study.

Similarly, the extent of benign disease of the bronchi such as bronchiectasis, can be better demonstrated selectively because bronchi are able to be completely filled with contrast material, even when they are filled with secretions.

Complications

The complications encountered to date include:

1. Subcutaneous emphysema (Figure 10): This occurs to some degree in about one-third of the patients and disappears without treatment in 24-48

DIAGNOSIS BY SELECTIVE BRONCHIAL CATHETERIZATION

ROCKOFF



FIG. 7. Abscess of superior segment of left lower lobe.

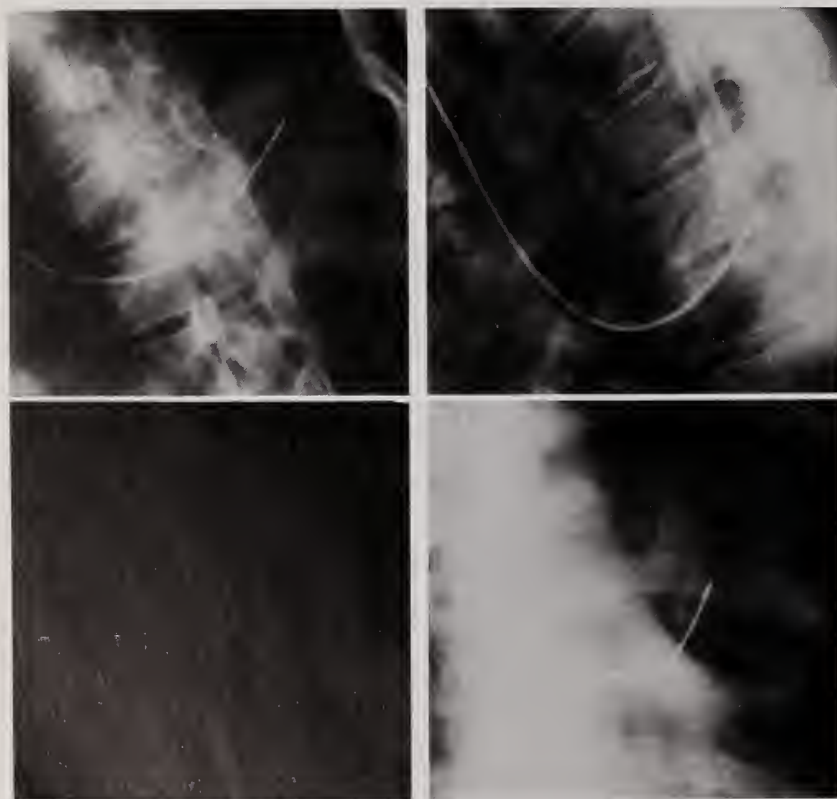


FIG. 8. Selective catheterization of cavity shown in Figure 7, which was drained and shown to be due to coagulase positive staphylococcus aureus.

hours. We have been successful in decreasing the incidence of this from about 75% to 30% by massaging the soft tissues over the cricothyroid membrane for a full five minutes at the end of the procedure.

2. Pneumomediastinum: This occurs occasionally in patients who develop subcutaneous emphysema and rarely causes symptoms.

3. Pneumothorax: I have seen two instances of this; one in a 16 year old girl who, four hours after the procedure had a coughing spell and spontaneously collapsed one lung. The relationship of this to the procedure is questionable. The other patient was a 57 year old female in whom a peripheral lesion was being brushed and in whom the tip of the brush apparently punctured the lung. Both patients were treated successfully with chest tubes.

4. Gross hemoptysis: Although blood streaking of the sputum is common during and following the procedure, in two patients with relatively central, necrotic carcinomas we have witnessed hemoptysis of over 10-25 cc. In both instances, this stopped spontaneously after having the patient lie on the side of the bleeding lung, with the head of the

FIG. 9. Semiselective failure of filling of apical-posterior segment of left upper lobe (Fig. 9A) which filled and is normal on selective catheterization (Fig. 9B) in patient with hemoptysis. This study permitted conservative management to be utilized.

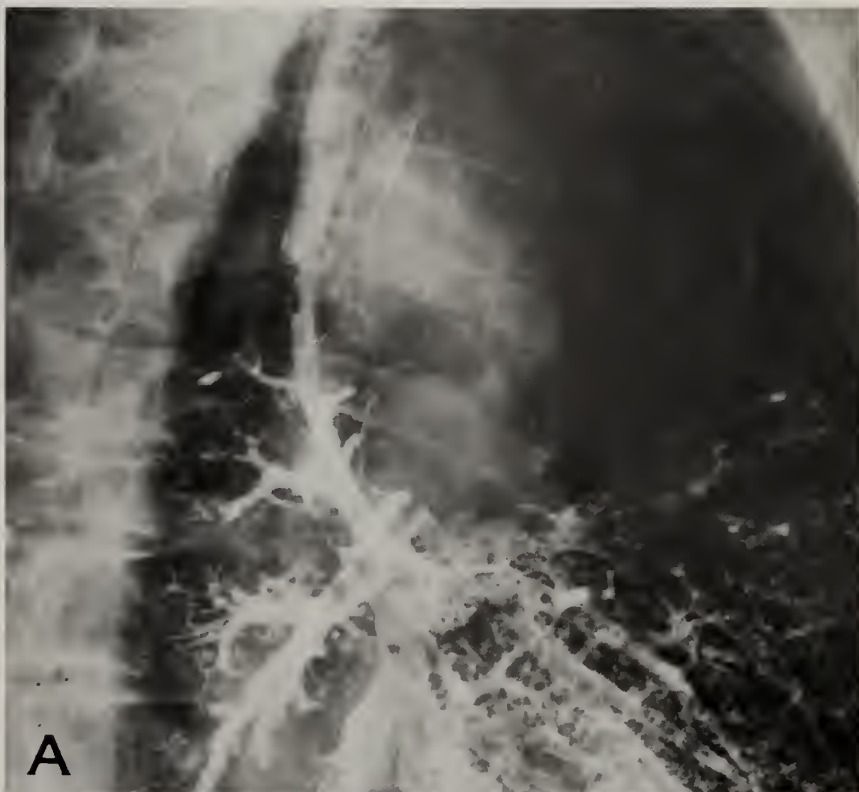


table tilted upward.

5. Infection: No infections in the neck have occurred. One patient did develop a soft tissue granuloma containing contrast material at the injection site (Figure 10). This was easily removed with a simple incision.

Summary and Conclusions

Selective bronchial catheterization under fluoroscopic control via the transcricothyroid approach has permitted, in over 500 patients:

- 1) The cytologic diagnosis of malignant lung disease which could not otherwise be diagnosed without surgery.
- 2) The specific diagnosis of inflammatory lung lesions without surgery.
- 3) The puncture of lung abscess, permitting specific therapy for infecting agents obtained, and possibly improving drainage.
- 4) The definitive clarification of bronchial abnormalities by selective bronchography.

The method itself has so far been unattended by any life threatening complications.



DIAGNOSIS BY SELECTIVE BRONCHIAL CATHETERIZATION

ROCKOFF



FIG. 10. Subcutaneous emphysema following transcricothyroid procedure. Patient also has sterile contrast material collection overlaying cricothyroid membrane. This was removed with incident through a simple small incision.

References

1. FENNESSY, J. J.: A Technique for the Selective Catheterization of Segmental Bronchi Using Arterial Catheters, *Am. J. Roentgen*, 1966, 96: 936.
2. FENNESSY, J. J.: Transbronchial Biopsy of Peripheral Lung Lesions, *Radiology*, 1967, 88: 878.
3. SARGENT, E. N. AND TURNER, A. F.: Percutaneous Transcricothyroid Membrane Selective Bronchography, *Am. J. Roentgenol*, 1968, 104: 792-801.
4. KYRIAKOS, M. AND ROCKOFF, S. D.: Brush Biopsy of Bronchial Carcinoid-A Source of Cytologic Error, *Acta Cytologica*, 1972, 16: 261.

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SPECIAL ARTICLE

Recent Advances in Respiratory Therapy

RONALD J. KARPICK, M.D.

Introduction

Because of the great changes which have occurred in inhalation therapy departments, the name is no longer appropriate. Respiratory therapy encompasses the widened scope of services, the better trained individuals and the greater responsibility exercised in the ventilatory care of hospitalized patients. The JCAH has introduced standards and the AMA has approved educational institutions for respiratory therapy. Therapeutic modalities now include the ultrasonic nebulizer, the use of PEEP, the use of IMV and the new endotracheal cuffs.

Within the past year or two, several advances have occurred in Respiratory Therapy. Four of these developments are briefly reviewed here, even though their ultimate place in treatment still needs to be more precisely defined.

Ultrasonic Nebulization

In the area of therapeutic methods, the most recent inhalant is ultrasonically nebulized mist. By means of a piezoelectronic crystal, electrical energy is converted into high frequency sound waves (1.35 megacycles) which in turn break water or a saline solution into very small droplets which become suspended in air. The particles of liquid water float in air: the water is

not converted into its gaseous phase as occurs with most humidifiers, and thus the quantity of water carried by the air is not a function of the air temperature. Whether inhaling water particles of the diameter which can reach the terminal bronchioles (5 microns) is beneficial is still a moot point. Probably there are many variables which affect the response and ultimate outcome, and as yet only a few have been defined. It has been demonstrated adequately that if the particulate water mist is inhaled through the nose, approximately 80% of the fluid will be deposited there. The nose is a truly effective filter. Whether there are any effects of this nasal deposition is yet unknown. It is of interest that nasally instilled isoproterenol decreases airway resistance within the lung.¹

If the ultrasonically produced mist is inhaled through the widely opened mouth, 40-60% of the mist enters the lower respiratory tract, even when the individual is specifically instructed to avoid deep breathing and breathholding.² It would be expected that these latter two procedures, which are used in the therapeutic administration of ultrasonic mist, would only enhance the deposition of fluid in the lower respiratory tract. The quantity of fluid delivered to the lung is small, less than 80 cc. in 24 hours continuous use.² However, even after shorter periods of time and thus less water deposition, many effects have been noted. Cough

is almost universally produced, especially if distilled water or 5% sodium chloride solutions are inhaled. Sputum is more frequently expectorated after inhaling these latter two compounds than with normal saline, so that this technique is only aggravating. Patients with inflamed bronchial trees, including asthmatics, may develop bronchospasm and an increase of airway resistance. This is due to bronchial smooth muscle constriction, can be prevented and treated with isoproterenol, and is not unique to water particles. It has also been described after inhaling tobacco smoke, citrate particles and cold air.^{3,5} Additionally, ultrasonic mist causes a decrease in vital capacity, a decrease in dynamic compliance, an increase in nonelastic resistance, and a fall in the arterial oxygen tension, with a widening of the alveolar-arterial oxygen gradient.^{4,6-8} These effects are probably related to the hydration of mucus, its movement in the bronchioles, and the bronchial smooth muscle contraction. How long these effects last and their clinical significance is yet unknown. The fall in the oxygen tension was greatest in patients with more normal pulmonary function, and in those with carbon dioxide retention and was minimized with the addition of intermittent positive pressure breathing.⁷ Mice experiments have shown that saline mist continuously inhaled for 72 hours produced inflammation and alveolar collapse and death of the mice. If the

RECENT ADVANCES IN RESPIRATORY THERAPY

KARPICK

mist was administered intermittently, there was no mortality.⁹ These observations have not been made in adult humans.

Although all of the data has not been collected, as with many forms of therapy, ultrasonic mist will probably be found effective for a defined segment of patients with lung disease. I believe that it is useful in patients with chronic bronchitis and bronchiectasis if administered after a bronchodilator, with a low concentration of mist (less than 3 cc/min.), using 0.45% or 0.9% sodium chloride solution, intermittently, and followed by chest physiotherapy. This would allow the hydrated, mobilized sputum to be moved out of the small airways into those from which it can be effectively drained and expectorated. As one author relates "the majority of patients under direct questioning felt that the treatment was beneficial. This subjective improvement was judged by a feeling of post treatment improvement of breathing and easier expectoration of sputum".⁷

Improved Endotracheal Cuffs

The other area of therapy in which many advances have been made is in the one of assisted or continuous ventilation, specifically with endotracheal cuffs, positive and expiratory pressure ventilation, and weaning. The types of endotracheal tube cuffs are increasing each day. Each manufacturer represents his tube to be the best. Fortunately, there is a growing body of data reviewing these cuffs and their effects on the tracheal mucosa: it has been demonstrated that the complications of intratracheal tubes are a consequence of the damage caused by the cuffs on the tracheal wall.¹⁰ The necrosis of mucosa and cartilage is caused by the occlusion of the blood vessels nourishing these tissues; thus, in a normotensive patient, the lateral

wall pressure exerted by the cuff becomes an important consideration. If this pressure is above the surrounding capillary pressure, tissue necrosis will ensue. It has been shown that the high pressure cuffs uniformly produce damage, and that large residual volume, large diameter low pressure cuffs do not if used properly.¹⁰ Unfortunately, not all of the cuffs so advertised are actually low pressure.¹¹ Wu has shown that the Lanz cuff with its attached pilot balloon is probably the best now available. Carroll and Grenvik caution that even these cuffs should be periodically checked with an aneroid pressure gauge to ensure they are expanded to the minimum "just seal" pressure, and if this exceeds 25 Torr to replace the cuff with a larger one.¹² A new concept in cuffs is the "parachute" self inflating cuff described by Finley and Abouav.¹³ This cuff is inflated by air moving in the trachea toward the mouth during the inspiratory phase of the ventilator. This allows the lateral wall pressure to be intermittent and it does not exceed 15 Torr. Theoretically, this would not cause tissue necrosis; however, there may be trouble in maintaining the tube within the trachea so that it does not plow into the mucosa, and in preventing aspiration. Further, *in vitro* and *in vivo* studies supported by autopsy and fiberoptic bronchoscopy data regarding these cuffs will be of interest.

PEEP

The concept of positive end expiratory pressure (PEEP) and continuous positive airway pressure (CPAP) has been an extremely important advance in the care of the patient with the adult respiratory distress syndrome. The reader is directed to several excellent reviews.¹⁴⁻¹⁸ The addition of a positive pressure to the airways during the entire respiratory cycle

apparently prevents airway closure, and allows better ventilation of the perfused alveoli with resultant increase in arterial oxygenation. There is an increase in the functional residual capacity and a decrease in the intrapulmonary blood shunt. Whether these changes help the patient is debatable. Lutch and Murray showed that PEEP is not particularly useful for patients with normal lungs or with chronic obstructive pulmonary diseases.¹⁹ Nicotra et al. and Kumar et al. studied patients with the adult respiratory distress syndrome and showed a decrease in the venous admixture, an increase in the venous oxygen content, and a persistence of a normal or elevated cardiac index.^{20,21} This type of treatment should not be applied to all patients requiring ventilatory assistance. It should be used in those patients with marked respiratory distress, with diffuse pulmonary infiltrates and stiff non-compliant lungs where arterial oxygen tension cannot be maintained above 50 mmHg with an inspired oxygen concentration of less than 50%. If the patient is already hypotensive, or has a small intravascular volume, one has to be prepared to expand the intravascular volume, as the initiation of either IPPB or PEEP may further decrease the cardiac output by interfering with venous filling of the heart. When PEEP is used, at a minimum, one has to follow the systemic blood pressure, the central venous pressure, the urine output and the arterial blood gas tensions. Optimally one would also like to follow the alveolar-arterial oxygen gradient, the central venous blood gas tensions, the cardiac output, the percentage venous admixture and the body weight. By these variables, it can be ascertained if PEEP is useful for the particular patient. They also may aid in the better definition of the patient most likely to benefit from PEEP.

Weaning

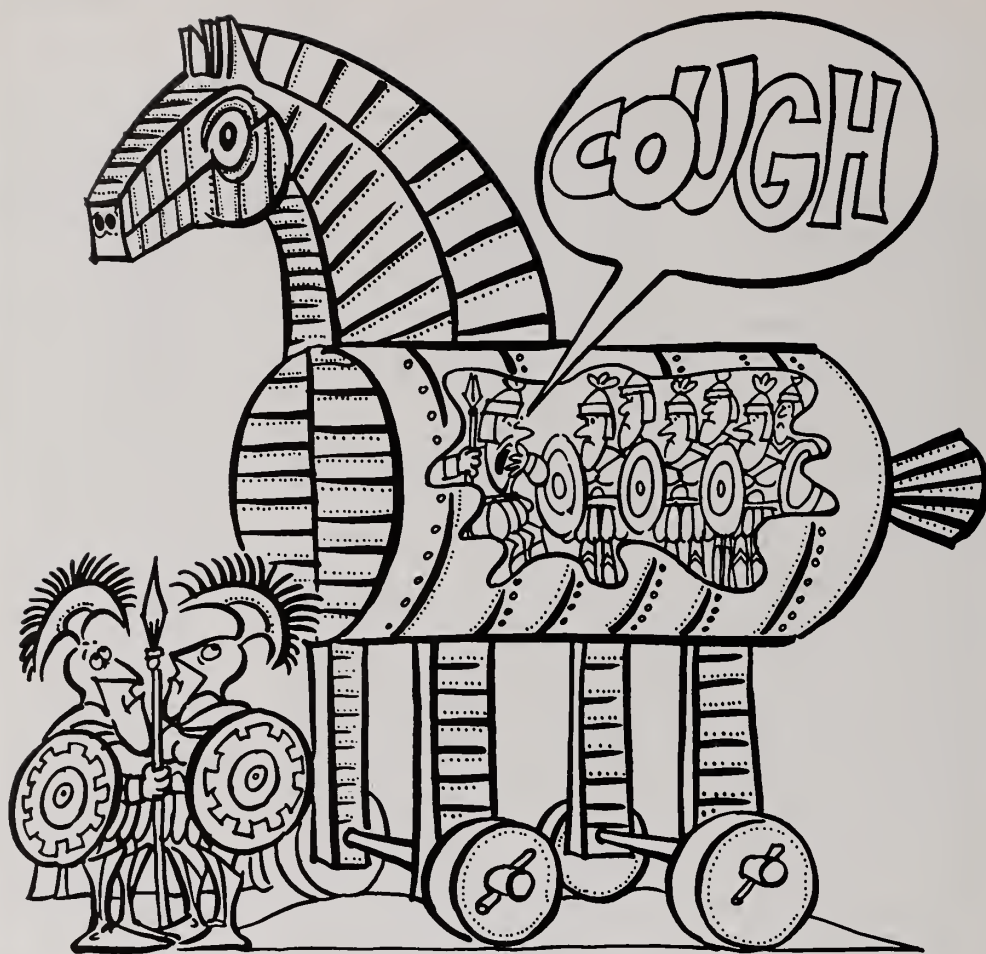
After the patient has been intubated with the properly cuffed endotracheal tube, and received the proper type of ventilatory assistance, he has to be weaned from the machine before convalescence can begin. Weaning is frequently stressful to the patient and the staff and is usually done in a sink-or-swim fashion with T-piece trials. If the patient's vital capacity is 15 cc. per Kg. body weight and the inspiratory force is at least 20 cm. of water pressure, the individual is a good candidate to commence weaning.^{2,2} However, even if the patient does not fulfill these minimal criteria, weaning can be done with the technique of intermittent mandatory ventilation (IMV) as described by Downs et al., Desautels et al. and Luedke et al., even if PEEP is required by the patient.^{2,3-2,5} This technique combines the Briggs T-piece adaptor and a unidirectional valve with the mechanical ventilator to permit spontaneous ventilation, while still delivering periodic breaths from the ventilator. The ventilator is adjusted to deliver a preset volume and a specific number of breaths per minute. This minute volume is delivered in addition to the patient's own spontaneous breathing. As the patient becomes stronger and is capable of doing more on his own, the number of present mandatory breaths can be decreased progressively to zero. If the patient fatigues, or becomes apneic, the machine would continue to deliver its preset minute volume in spite of no spontaneous breathing. By this method precipitous changes in pO_2 and pCO_2 would be avoided. Since there are no equipment changes, the fear of the patient should be minimized, perhaps making the weaning process go even more smoothly.

References

1. COHEN, B. M.: The Nasal Respiratory Handicap of Expiratory Airflow Disease, *Respiration*, 1970, 27, 406.
2. WOLFSDORF, J., SWIFT, D. L., AVERY, M. E.: Mist Therapy Reconsidered: An Evaluation of the Respiratory Deposition of Labelled Water Aerosols Produced by Jet and Ultrasonic Nebulizers, *Pediatrics*, 1969, 43, 799.
3. CHENEY, F. W. JR., BUTLER, J.: The Effects of Ultrasonically Produced Aerosols On Airway Resistance in Man, *Anesthesiology*, 1968, 29, 1099.
4. MALIK, S. K., JENKINS, D. E.: Alterations in Airway Dynamics Following Inhalation of Ultrasonic Mist, *Chest*, 1972, 62, 660.
5. WIDDICOMBE, J. G.: The Regulation of Bronchial Calibre, in C. G. Caro (Editor), *Advances in Respiratory Physiology*, Arnold, London, 1968, 48.
6. MUIR, D. C.: Physiological Aspects of Ultrasonic Aerosols, *Respiration*, 1970, 27 Suppl, 185.
7. TAGUCHI, J. T.: Effect of Ultrasonic Nebulization on Blood Gas Tensions in Chronic Obstructive Lung Disease, *Chest*, 1971, 60, 356.
8. PFLUG, A. E., CHENEY, F. W. JR., BUTLER, J.: The Effects of an Ultrasonic Aerosol on Pulmonary Mechanics and Arterial Blood Gases in Patients with Chronic Bronchitis, *American Review Respiratory Diseases*, 1970, 101, 710.
9. MODELL, J. H., SMITH, B. E., WILLIAM, H. D., WEIBLEY, J. C., JALOWAYSKI, A.: Tolerance of Mice to Ultrasonic Aerosol Exposure, *J. Diseases Children*, 1968, 115, 322.
10. COOPER, J. D., GRILLO, H. C.: Analysis of Problems Related to Cuffs on Intratracheal Tubes, *Chest*, 1972, 62 Suppl., 21 S.
11. WU, W., LIM, I., SIMPSON, F. A., TURNDOR, H.: Pressure Dynamics of Endotracheal and Tracheostomy Cuffs, *Critical Care Medicine*, 1973, 1, 197.
12. CARROLL, R. G., GRENVIK, A.: Proper Use of Large Diameter, Large Residual Volume Cuffs, *Critical Care Medicine*, 1973, 1, 153.
13. FINLEY, T., ABOUAY, J.: Pressure Characteristics of a "Parachute" Self Inflating Intratracheal Cuff, *American Review Respiratory Diseases*, 1973, 107, 1071.
14. PETTY, T. L., ASHBAUGH, D. G.: The Adult Respiratory Distress Syndrome, *Chest*, 1971, 60, 233.
15. PONTOPPIDAN, H., GEFFIN, B., LOWENSTEIN, E.: Acute Respiratory Failure in the Adult, *New England J. Medicine*, 1972, 287, 690, 743, 799.
16. ASHBAUGH, D. G., PETTY, T. L.: Positive End-Expiratory Pressure: Physiology, Indications and Contraindications, *J. Thoracic and Cardiovascular Surgery*, 1973, 65, 165.
17. SUGARMAN, H. J., ROGERS, R. M., MILLER, L. D.: Positive End Expiratory Pressure: Indications and Physiologic Considerations, *Chest*, 1972, 62 Suppl., 86S.
18. LEFTWICH, E. L., WITORSCH, R. J., WITORSCH, P.: Positive End-Expiratory Pressure in Refractory Hypoxemia. A Critical Evaluation, *Annals Internal Medicine*, 1973, 79, 187.
19. LUTCH, J. S., MURRAY, J. F.: Continuous Positive Pressure Ventilation: Effects on Systemic Oxygen Transport and Tissue Oxygenation, *Annals Internal Medicine*, 1972, 76, 193.
20. NICOTRA, N. B., STEVENS, P. M., VIROSLAV, J., ALVAREZ, A.: Physiologic Evaluation of Positive End Expiratory Pressure Ventilation, *Chest*, 1973, 64, 10.
21. KUMAR, A., FALKE, K. J., GEFFIN, B., ALDREDGE, C. F., LAVER, M. B., LOWENSTEIN, E., PONTOPPIDAN, H.: Continuous Positive Pressure Ventilation in Acute Respiratory Failure, *New England J. Medicine*, 1970, 283, 1430.
22. BROWNE, A. G., PONTOPPIDAN, H., CHIANG, H.: Physiological Criteria for Weaning Patients from Prolonged Artificial Ventilation, *ASA Abstracts of Scientific Papers*, 1972, 6.
23. DOWNS, J. B., KLEIN, E., DESAUTELS, D., MODELL, J. H., KIRBY, R. R.: Intermittent Mandatory Ventilation: A New Approach to Weaning Patients from Mechanical Ventilators, *Chest*, 1973, 64, 331.
24. DESAUTELS, D. A., BARTLETT, J. L.: Methods of Administering Intermittent Mandatory Ventilation, to be published.
25. LUEDKE, J., KOSMATKA, A.: A New Method of Weaning from Respirator Support, *Respiratory Care*, 1973, 18, 561.

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Triaminic, 25 mg. (phenylpropanolamine hydrochloride, 12.5 mg.;
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Remember, you're hiring her
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For an organization supposedly opposed to change, the AMA has made a lot of changes.

One of the most significant was the addition of an important new voice in the AMA—that of interns and residents. For the first time, these young physicians have not only a voice but also a vote in helping shape AMA policies.

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That's not all. In another important change, the AMA's council-committee structure has been streamlined. Some councils and committees have been dropped. Others have been made more efficient by reducing their size to seven members for councils and five for committees. And to permit more frequent infusion of new

members and ideas, maximum tenure of service has been reduced to seven and five years, respectively.

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**Fast relief of nasal congestion
and hypersecretion*
with convenient b.i.d. dosage.**

Before prescribing, see complete prescribing information in SK&F literature or *PDR*. The following is a brief summary.

* Indications

Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

Possibly effective: For relief of upper respiratory tract congestion and hypersecretion associated with vasomotor rhinitis and allergic rhinitis, and for prolonged relief.

Lacking in substantial evidence of effectiveness: For relief of nasal congestion and hypersecretion associated with the common cold and sinusitis.

Final classification of the less-than-effective indications requires further investigation.

Contraindications: Hypersensitivity to any component; concurrent MAO inhibitor therapy; severe hypertension; bronchial asthma; coronary artery disease; stenosing peptic ulcer; pyloroduodenal or bladder neck obstruction. Children under 6.

Warnings: Caution patients about activities requiring alertness (e.g., operating vehicles or machinery). Warn patients of possible additive effects with alcohol and other CNS depressants.

Usage in Pregnancy: In pregnancy, nursing mothers and women who might bear children, weigh potential benefits against hazards. Inhibition of lactation may occur.

Effect on PBI Determination and I^{131} Uptake: Isopropamide iodide may alter PBI test results and will suppress I^{131} uptake. Substitute thyroid tests unaffected by exogenous iodides.

Precautions: Use cautiously in persons with cardiovascular disease, glaucoma, prostatic hypertrophy, hyperthyroidism.

Adverse Reactions: Drowsiness, excessive dryness of nose, throat or mouth; nervousness; or insomnia. Also, nausea, vomiting, epigastric distress, diarrhea, rash, dizziness, weakness, chest tightness, angina pain, abdominal pain, irritability, palpitation, headache, incoordination, tremor, dysuria, difficulty in urination, thrombocytopenia, leukopenia, convulsions, hypertension, hypotension, anorexia, constipation, visual disturbances, iodine toxicity (acne, parotitis).

Supplied: Bottles of 50 capsules.

SK&F Smith Kline & French Laboratories
Division of SmithKline Corporation, Philadelphia, Pa. 19101

Each Spansule® capsule contains 8 mg. Teldrin® (brand of chlorpheniramine maleate); 50 mg. phenylpropanolamine hydrochloride; 2.5 mg. isopropamide, as the iodide.





The irritations of man's day are often reflected in his gut.

The causes of irritable colon and the diarrheal symptoms that often accompany it can be as diverse as the systemic and emotional irritations man is faced with daily.

Although the mucoid nature of stools and the occurrence of diarrheal episodes coincident with times of emotional stress may be valuable clues to the functional nature of the disorder, irritable colon must often be diagnosed by exclusion. Such diagnostic exploration takes time. Discovery of the nature of any emotional problems may take more. During that time, Lomotil® is an ideal agent for controlling diarrheal symptoms.

Lomotil tablets are small, easy to carry and easy to take. They act promptly and effectively. Secondary effects are relatively infrequent and, once the first force of the diarrhea is controlled, maintenance is frequently effective on as little as one fourth of the initial dosage.

These same characteristics make Lomotil useful in controlling the diarrhea associated with gastroenteritis, antibiotic therapy and acute infections.



IMPORTANT INFORMATION: This is a Schedule V substance by Federal law; diphenoxylate HCl is chemically related to meperidine. In case of overdosage or individual hypersensitivity, reactions similar to those after meperidine or morphine overdosage may occur; treatment is similar to that for meperidine or morphine intoxication (prolonged and careful monitoring). Respiratory depression may recur in spite of an initial response to Nalline® (nalorphine HCl) or may be evidenced as late as 30 hours after ingestion. LOMOTIL IS NOT AN INNOCUOUS DRUG AND DOSAGE RECOMMENDATIONS SHOULD BE STRICTLY ADHERED TO, ESPECIALLY IN CHILDREN, THIS MEDICATION SHOULD BE KEPT OUT OF REACH OF CHILDREN.

Indications: Lomotil is effective as adjunctive therapy in the management of diarrhea.

Contraindications: In children less than 2 years, due to the decreased safety margin in younger age groups, and in patients who are jaundiced or hypersensitive to diphenoxylate HCl or atropine.

Warnings: Use with caution in young children, because of variable response, and with extreme caution in patients with cirrhosis and other advanced hepatic disease or abnormal liver function tests, because of possible hepatic coma. Diphenoxylate HCl may potentiate the action of barbiturates, tranquilizers and alcohol. In theory, the concurrent use with monoamine oxidase inhibitors could precipitate hypertensive crisis.

Usage in pregnancy: Weigh the potential benefits against possible risks before using during pregnancy, lactation or in women of childbearing age. Diphenoxylate HCl and atropine are secreted in the breast milk of nursing mothers.

Precautions: Addiction (dependency) to diphenoxylate HCl is theoretically possible at high dosage. Do not exceed recommended dosages. Administer with caution to patients receiving addicting drugs or known to be addiction prone or having a history of drug abuse. The subtherapeutic amount of atropine is added to discourage deliberate overdosage; strictly observe contraindications, warnings and precautions for atropine; use with caution in children since signs of atropinism may occur even with the recommended dosage.

Adverse reactions. Atropine effects include dryness of skin and mucous membranes, flushing and urinary retention. Other side effects with Lomotil include nausea, sedation, vomiting, swelling of the gums, abdominal discomfort, respiratory depression, numbness of the extremities, headache, dizziness, depression, malaise, drowsiness, coma, lethargy, anorexia, restlessness, euphoria, pruritus, angioneurotic edema, giant urticaria and paralytic ileus.

Dosage and administration: Lomotil is contraindicated in children less than 2 years old. Use only Lomotil liquid for children 2 to 12 years old. For ages 2 to 5 years, 4 ml. (2 mg.) t.i.d.; 5 to 8 years, 4 ml. (2 mg.) q.i.d.; 8 to 12 years, 4 ml. (2 mg.) 5 times daily; adults, two tablets (5 mg.) t.i.d. to two tablets (5 mg.) q.i.d. or two regular teaspoonfuls (10 ml., 5 mg.) q.i.d. Maintenance dosage may be as low as one fourth of the initial dosage. Make downward dosage adjustment as soon as initial symptoms are controlled.

Overdosage: Keep the medication out of the reach of children since accidental overdosage may cause severe, even fatal, respiratory depression. Signs of overdosage include flushing, lethargy or coma, hypotonic reflexes, nystagmus, pinpoint pupils, tachycardia and respiratory depression which may occur 12 to 30 hours after overdose. Evacuate stomach by lavage, establish a patent airway and, when necessary, assist respiration mechanically. Use a narcotic antagonist in severe respiratory depression. Observation should extend over at least 48 hours.

Dosage forms: Tablets, 2.5 mg. of diphenoxylate HCl with 0.025 mg. of atropine sulfate. Liquid, 2.5 mg. of diphenoxylate HCl and 0.025 mg. of atropine sulfate per 5 ml. A plastic dropper calibrated in increments of ½ ml. (total capacity, 2 ml.) accompanies each 2-oz. bottle of Lomotil liquid.

Lomotil®

TABLETS/LIQUID

Each tablet and each 5 ml. of liquid contain:
diphenoxylate hydrochloride . . . 2.5 mg.
(Warning: May be habit forming)
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takes care of the gut issue
in irritable colon

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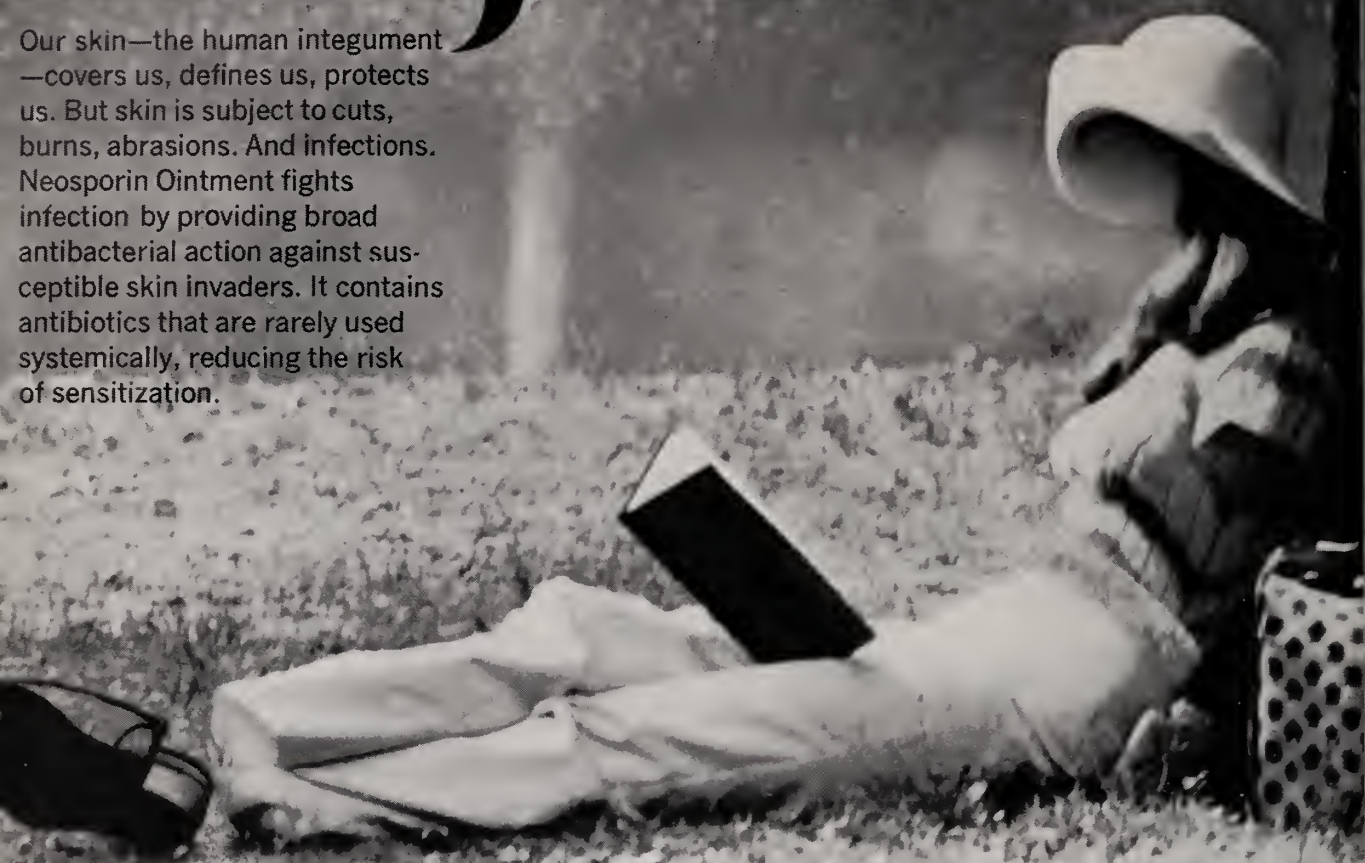
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Integument!

Our skin—the human integument—covers us, defines us, protects us. But skin is subject to cuts, burns, abrasions. And infections. Neosporin Ointment fights infection by providing broad antibacterial action against susceptible skin invaders. It contains antibiotics that are rarely used systemically, reducing the risk of sensitization.



INDICATIONS: *Therapeutically*, used as an adjunct to appropriate systemic therapy for topical infections, primary or secondary, due to susceptible organisms, as in:

- infected burns, skin grafts, surgical incisions, otitis externa
- primary pyodermas (impetigo, ecthyma, sycosis vulgaris, paronychia)
- secondarily infected dermatoses (eczema, herpes, and seborrheic dermatitis)
- traumatic lesions, inflamed or suppurating as a result of bacterial infection.

Prophylactically, the ointment may be used to prevent bacterial contamination in burns, skin grafts, incisions, and other clean lesions. For abrasions, minor cuts and wounds accidentally incurred, its use may prevent the development of infection and permit wound healing.

CONTRAINDICATIONS: Not for use in the external ear canal if the eardrum is perforated. This product is contraindicated in those individuals who have shown hypersensitivity to any of the components.

PRECAUTION: As with other antibiotic preparations, prolonged use may result in overgrowth of nonsusceptible organisms and/or fungi. Appropriate measures should be taken if this occurs. Articles in the current medical literature indicate an increase in the prevalence of persons allergic to neomycin. The possibility of such a reaction should be borne in mind.

Complete literature available on request from Professional Services Dept. PML.

NEOSPORIN[®] Ointment

(POLYMYXIN B-BACITRACIN-NEOMYCIN)

Each gram contains: Aerosporin[®] brand Polymyxin B Sulfate 5,000 units; zinc bacitracin 400 units; neomycin sulfate 5 mg. (equivalent to 3.5 mg. neomycin base); special white petrolatum q.s. In tubes of 1 oz. and ½ oz. and ¼ oz. (approx.) foil packets.



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POST GRADUATE EDUCATION

PRUDENT NUTRITION AND THE PILL

Joseph Giere, M.D.
Georgetown U. School of Medicine

During a recent twelve month period, one major area drug chain sold one half million one month packets of oral contraceptives. This commonly used drug has been the subject of much press and medical discussion and debate, and the major serious (albeit rare) side effects of deep vein thrombophlebitis, pulmonary embolism and cerebrovascular accidents are now well known. Several recent studies have suggested another possible side effect with far reaching consequences in the possible link between the oral contraceptive user's psyche and her overall nutrition. Urine measurements of female users of oral contraceptives and of a male who for five weeks used a daily dose of 0.1 mgm ethinyl estradiol, one of the estrogen compounds used in the pill, show a deficiency of vitamin B₆, pyridoxine. Lack of pyridoxine alters the metabolism of serotonin. Low levels of serotonin have been linked to psychogenic changes primarily depression, fatigue, emotional lability and irritability. The normal daily requirement of pyridoxine is 2 mgm daily. Some clinicians have given 50–100 mgm daily to oral contraceptive users who complain of psychogenic changes. They assert there is prompt almost complete disappearance of these symptoms in the majority of their patients. They advocate the routine use of vitamin B₆ with oral contraceptives.

Low serum folic acid levels are a relatively common vitamin deficiency in man. In several studies, long term use of oral contraceptives have been associated with low serum folate levels possibly by interfering with absorption. It is feared that patients who discontinue oral contraception for pregnancy may be depleted of this vital nutrient at a particularly critical time in an early pregnancy.

Vitamin B₁₂ levels may also be lower in pill versus non pill users. Clinical disease has not been reported. It is feared that nutritionally borderline women may be tipped over into clinical disease while using oral contraceptives. These studies are *suggestive* rather than definitive. We need further *unequivocal data* from which to draw final conclusions. It's not unreasonable, however, for physicians to reinforce good diet habits and food intake for patients who seek prescriptions for oral contraceptive therapy and to prescribe vitamin preparations for any nutritionally borderline pill users.

What's on your patient's face...

may be more important than his chief complaint

Patient P.T.* seen on 3/29/67 shows typical lesions of moderately severe keratoses. Note residual scarring on ridge of nose from previous cryosurgical and electrosurgical procedures.



Patient P.T.* seen on 6/12/67, seven weeks after discontinuation of 5% FU cream. Reaction has subsided. Residual scarring not seen except that due to prior surgery. Inflammation has cleared and face is clear of keratotic lesions.

*Data on file,
Hoffmann-La Roche
Inc., Nutley, N.J



The lesions on his face are solar/actinic— so-called "senile" keratoses... and they may be premalignant.

Solar, actinic or senile keratoses

These lesions may be called by several names, but they usually can be identified by the following characteristics. The typical lesion is flat or slightly elevated, of a brownish or reddish color, papular, dry, rough, adherent and sharply defined. They commonly occur as multiple lesions, chiefly on the exposed portions of the skin.

Sequence of therapy— selectivity of response

After several days of therapy with Efudex® (fluorouracil), erythema may begin to appear in the area of the lesions; this reaction usually reaches its height of unsightliness and discomfort within two weeks, declining after discontinuation of therapy. This reaction occurs in affected areas. Since the response is so predictable, lesions that do not respond should be biopsied.

Acceptable results

Treatment with Efudex provides highly favorable cosmetic results. Incidence of scarring is low. This is particularly important with multiple facial lesions. Efudex should be applied with care near the eyes, nose and mouth.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Multiple actinic or solar keratoses.

Contraindications: Patients with known hypersensitivity to any of its components.

Warnings: If occlusive dressing used, may increase inflammatory reactions in adjacent normal skin. Avoid prolonged exposure to ultraviolet rays. Safe use in pregnancy not established.

Precautions: If applied with fingers, wash hands immediately. Apply with care near eyes, nose and mouth. Lesions failing to respond or recurring should be biopsied.

Adverse Reactions: Local—pain, pruritus, hyperpigmentation and burning at application site most frequent; also dermatitis, scarring, soreness and tenderness. Also reported—insomnia, stomatitis, suppuration, scaling, swelling, irritability, medicinal taste, photosensitivity, lacrimation, leukocytosis, thrombocytopenia, toxic granulation and eosinophilia.

Dosage and Administration: Apply sufficient quantity to cover lesion twice daily with nonmetal applicator or suitable glove. Usual duration of therapy is 2 to 4 weeks.

How Supplied: Solution, 10-ml drop dispensers—containing 2% or 5% fluorouracil on a weight/weight basis, compounded with propylene glycol, tris(hydroxymethyl)-aminomethane, hydroxypropyl cellulose, parabens (methyl and propyl) and disodium edetate.

Cream, 25-Gm tubes—containing 5% fluorouracil in a vanishing cream base consisting of white petrolatum, stearyl alcohol, propylene glycol, polysorbate 60 and parabens (methyl and propyl).



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110

This patient's lesions were resolved with

Efudex® fluorouracil/Roche®

5% cream/solution...a Roche exclusive

ECG PROBLEMS

HISTORY: A sixty-seven-year old, white female with a long history of heart disease and left bundle branch block. The first tracing was taken the day of admission for congestive heart failure. The second was taken seven days later when she developed severe chest pain.

(for interpretation see page 171)

Figure 1

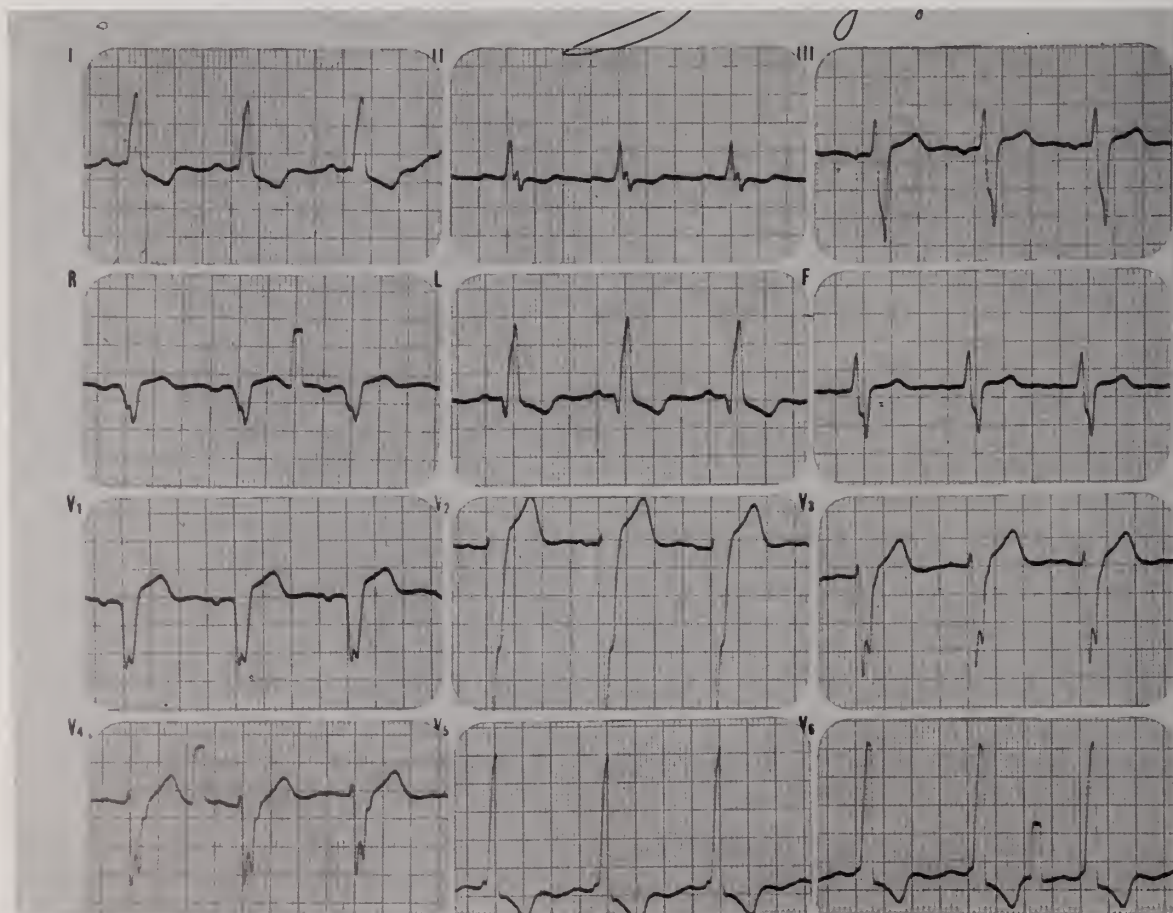
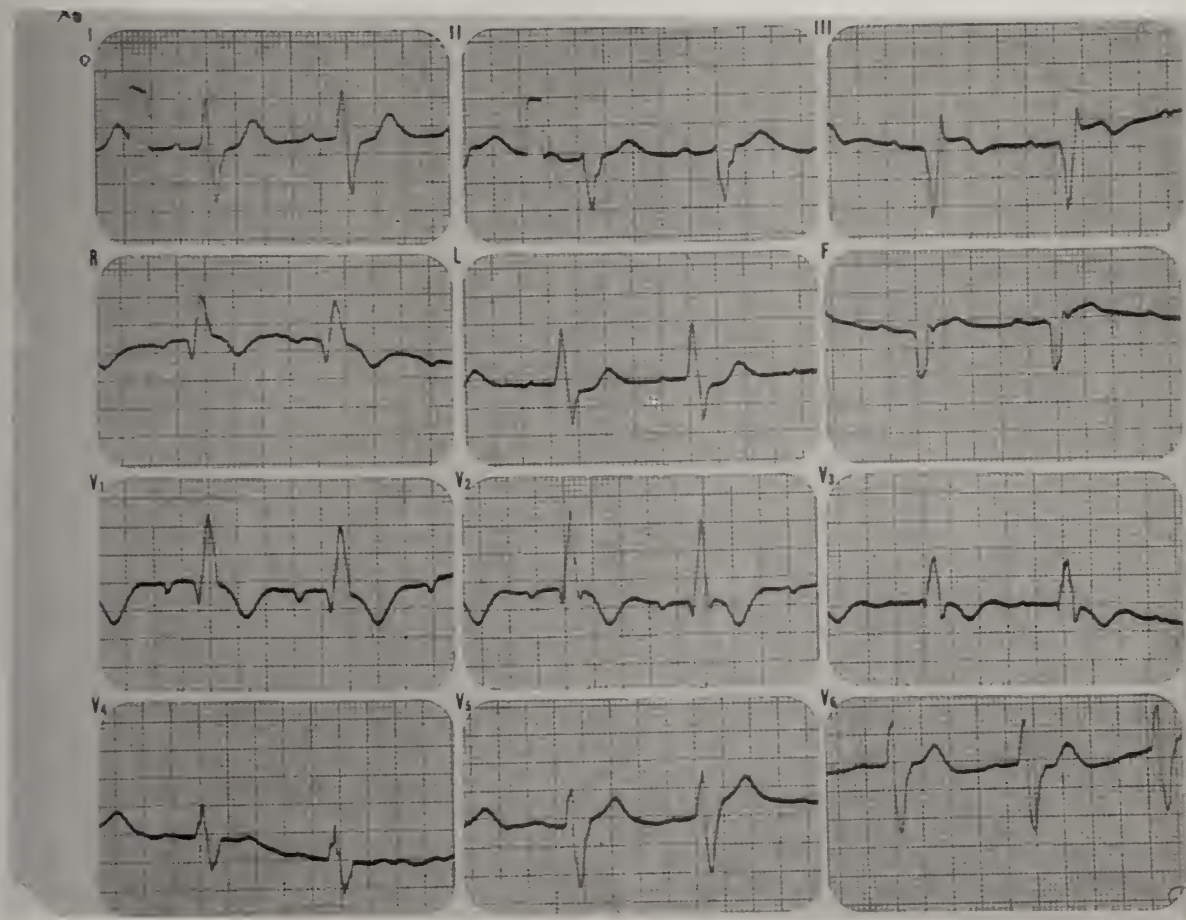


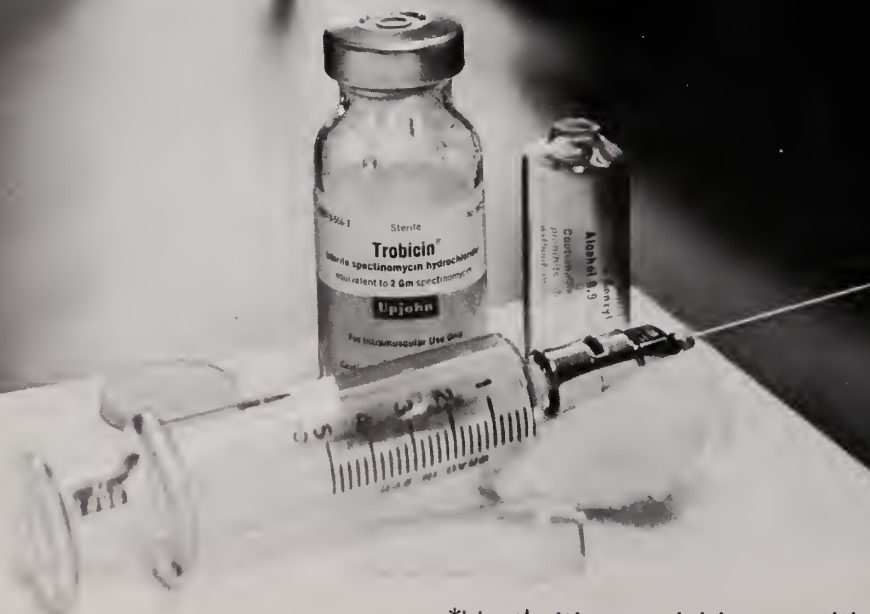
Figure 2



acute gonorrhea

This patient
just received
an effective, private,
physician-controlled
treatment.

It took just one short visit.



*Urethritis, cervicitis, proctitis when due
to susceptible strains of *N. gonorrhoeae*

Trobicin—The advantage of injectable therapy.

Once Trobicin is injected, treatment is usually complete; there can be no problems with patients sharing, skipping, skipping or forgetting medication.

Trobicin—The aspect of privacy.

There are no prescriptions to fill, no capsules to take. Neither family, friends nor co-workers need know or suspect the patient's problem.

Trobicin—Indication and dosage.

Spectinomycin is indicated only for use in acute urethritis and proctitis in the male and acute cervicitis and/or proctitis in the female when due to susceptible strains of *N. gonorrhoeae*. The usual dosage for Trobicin in adult males is 2 grams intramuscularly[†]; 4 grams intramuscularly in females.

Trobicin—Not effective for syphilis.

Trobicin is not effective for any stage of syphilis. Trobicin may mask or delay the symptoms of incubating syphilis. If concurrent syphilis is suspected, follow the patient serologically for at least 3 months. Patients with syphilis should receive adequate specific anti-syphilitic therapy with an appropriate antibiotic. Trobicin is contraindicated in patients previously found hypersensitive to it.

Intramuscular

...and **Trobicin**[®] 2 gm and 4 gm vials sterile spectinomycin hydrochloride

Sterile Trobicin

Sterile Trobicin (spectinomycin hydrochloride)
— For Intramuscular Injection:

2 gm vials containing 5 ml when reconstituted with diluent.

4 gm vials containing 10 ml when reconstituted with diluent.

An aminocyclitol antibiotic active *in vitro* against most strains of *Neisseria gonorrhoeae* (MIC 7.5 to 20 mcg/ml). Definitive *in vitro* studies have shown no cross resistance of *N. gonorrhoeae* between spectinomycin and penicillin.

Indications: Acute gonorrheal urethritis and proctitis in the male and acute gonorrheal cervicitis and proctitis in the female when due to susceptible strains of *N. gonorrhoeae*.

Contraindications: Contraindicated in patients previously found hypersensitive to spectinomycin.

Warnings: Not indicated for the treatment of syphilis. Antibiotics used to treat gonorrhea may mask or delay the symptoms of incubating syphilis. Patients should be carefully examined and monthly serological follow-up for at least 3 months should be instituted if the diagnosis of

syphilis is suspected.

Safety for use in infants, children and pregnant women has not been established.

Precautions: The usual precautions should be observed with atopic individuals. Clinical effectiveness should be monitored to detect evidence of development of resistance by *N. gonorrhoeae*.

Adverse reactions: The following reactions were observed during the single-dose clinical trials: soreness at the injection site, urticaria, dizziness, nausea, chills, fever and insomnia. During multiple-dose subchronic tolerance studies in normal human volunteers, the following were noted: a decrease in hemoglobin, hematocrit and creatinine clearance; elevation of alkaline phosphatase, BUN and SGPT. In single- and multiple-dose studies in normal volunteers, a reduction in urine output was noted. Extensive renal function studies demonstrated no consistent changes indicative of renal toxicity.

Dosage and administration: Keep at 25° C and use within 24 hours after reconstitution with diluent.

Male—Inject 5 ml intramuscularly for a 2 gram dose. Patients with gonorrheal proctitis and patients being re-treated after failure of previous antibiotic therapy should receive 4 grams (10 ml). In geographic areas where antibiotic resistance is known to be prevalent, initial treatment with 4 grams (10 ml) intramuscularly is preferred.

Female—Inject 10 ml intramuscularly for a 4 gram dose.

How supplied: Vials, 2 and 4 grams—with ampoule of Bocteriostatic Water for Injection with Benzyl Alcohol 0.9% w/v. Reconstitution yields 5 and 10 ml respectively with a concentration of 400 mg spectinomycin per ml (as the hydrochloride). For intramuscular use only. **Susceptibility Powder**—for testing *in vitro* susceptibility of *N. gonorrhoeae*.

Caution: Federal law prohibits dispensing without prescription.

For additional product information see your Upjohn representative or consult the package insert.

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MED B-5-S (IMBR-1)
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[†]For patients with gonorrheal proctitis and for patients in geographic areas where antibiotic resistance is known to be prevalent, initial treatment with 4 grams is preferred.



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Indications: SYNTHROID (sodium levothyroxine) is specific replacement therapy for diminished or absent thyroid function resulting from primary or secondary atrophy of the gland, congenital defect, surgery, excessive radiation, or antithyroid drugs. Indications for SYNTHROID (sodium levothyroxine) **Tablets** include myxedema, hypothyroidism without myxedema, hypothyroidism in pregnancy, pediatric and geriatric hypothyroidism, hypopituitary hypothyroidism, simple (nontoxic) goiter, and reproductive disorders associated with hypothyroidism. SYNTHROID (sodium levothyroxine) **for Injection** is indicated for intravenous use in myxedematous coma and other thyroid dysfunctions where rapid replacement of the hormone is required. The injection is also indicated for intramuscular use in cases where the oral route is suspect or contraindicated due to existing conditions or to absorption defects, and when a rapid onset of effect is not desired.

Precautions: As with other thyroid preparations, an overdosage of SYNTHROID (sodium levothyroxine) may cause diarrhea or cramps, nervousness, tremors, tachycardia, vomiting and continued weight loss. These effects may begin after four or five days or may not become apparent for one to three weeks. Patients receiving the drug should be observed closely for signs of thyrotoxicosis. If indications of overdosage appear, discontinue medication for 2-6 days, then resume at a lower dosage level. In patients with diabetes mellitus, careful observations should be made for changes in insulin or other antidiabetic drug dosage requirements. If hypothyroidism is accompanied by adrenal insufficiency, such as Addison's Disease (chronic adrenocortical insufficiency), Simmonds's Disease (panhypopituitarism) or Cushing's syndrome (hyperadrenalism), these dysfunctions must be corrected prior to and during SYNTHROID (sodium levothyroxine) administration. The drug

should be administered with caution to patient with cardiovascular disease; development of chest pains or other aggravations of cardiovascular disease requires a reduction in dosage.

Contraindications: Thyrotoxicosis, acute myocardial infarction. **Side effects:** The effects of SYNTHROID (sodium levothyroxine) therapy are slow in being manifested. Side effects, when they do occur, are secondary to increased rates of body metabolism; sweating, heart palpitations with or without pain, leg cramps, and weight loss. Diarrhea, vomiting, and nervousness have also been observed. Myxedematous patients with heart disease have died from abrupt increase in dosage of thyroid drugs. Careful observation of the patient during the beginning of any thyroid therapy will alert the physician to any untoward effects.

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1 *Synthroid* is T₄.

2 Because T₄ converts to T₃ at the cellular level, it provides full thyroid replacement at maintenance doses.^{1, 2}

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6 *Synthroid* is the most prescribed brand name of thyroid in the U.S. and Canada.

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dosage may be increased to 0.05 mg. after two weeks and to 0.1 mg. at the end of a second two weeks. The daily dose may be further increased at two-month intervals by 0.1 mg. until the optimum maintenance dose is reached (0.1-1.0 mg. daily).

Supplied: Tablets: 0.025 mg., 0.05 mg., 0.1 mg., 0.15 mg., 0.2 mg., 0.3 mg., 0.5 mg., scored and color-coded, in bottles of 100, 500, and 1000. Injection: 500 mcg. lyophilized active ingredient and 10 mg. of Mannitol, U.S.P., in 10 ml. single-dose vial, with 5 ml. vial of Sodium Chloride Injection, U.S.P., as a diluent. SYNTHROID (sodium levothyroxine) for Injection may be administered intravenously utilizing 200-400 mcg. of a solution containing 100 mcg. per ml. If significant improvement is not shown the following day, a repeat injection of 100-200 mcg. may be

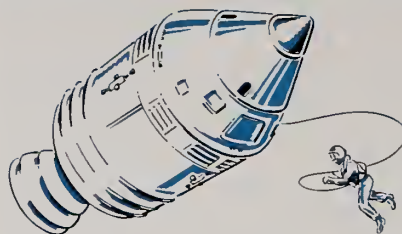
1. Braverman, L. E., Ingbar, S. H., and Sterling, K.: Conversion of Thyroxine (T₄) to Triiodothyronine (T₃) in Athyreotic Human Subjects, *J. Clin. Invest.* 49:855-64, 1970.

2. Surks, M. I., Schadow, A. R., and Oppenheimer, J. H.: A New Radioimmunoassay for Plasma L-Triiodothyronine: Measurements in Thyroid Disease and in Patients Maintained on Hormonal Replacement. *J. Clin. Invest.* 51:3104-13, 1972.



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BOOK REVIEWS

Genetic Control of Immune Responsiveness.

HUGO O. McDEVITT AND MAURICE LANDY,
Editors. Price, \$19.50. Pp. 469. New York: Academic
Press, Inc., 1973.

In 1909, Sir Archibald Garrod published the monograph, *Inborn Errors of Metabolism*. That book wedded Mendelian genetics with clinical medicine. Physicians now recognize that many inherited disorders result from a single gene defect. Expression of diseases with a recessive inheritance pattern depends on the genome being homozygous at a single allele, e.g. ss for the beta chain in sickle cell disease. Many diseases with a familial tendency such as diabetes, rheumatoid arthritis and others, do not fit Mendelian patterns of inheritance. The first breakthrough in elucidating the genetics of these diseases has come in the studies of leukemia in inbred mice. Frank Lilly and others have shown in a series of very elegant but complicated studies that the production of erythroleukemia in mice depends on the interaction of two viruses and at least three different unlinked genes, i.e. not on the same chromosome. We now have an animal model for understanding the multigenic control of disease. The leukemia situation is discussed at length in the book, *Genetic Control of Immune Responsiveness*, because one of the genes involved appears to be linked to the gene controlling the animal's ability to make antibodies. Mice capable of mounting an immune response against the virus do not get leukemia.

This text is the proceeding of a conference held at Brook Lodge in the Spring of 1972. Most of the foremost investigators in this field were present. The articles and discussions are in depth and current. There are thorough discussions of the genetics and relationships among cell surface antigens and immune responsiveness. Recently it has been shown that populations with certain HL-A antigens are more inclined to develop psoriasis. Some data suggests a linkage between systemic lupus erythematosus, or Hodgkin's Disease, or myeloma, and particular cell surface antigens. The implication of these relationships are discussed at length.

For the man in the lab this book summarizes recent developments in immunology that may become as important as the observations of Garrod two generations ago. For the practicing physician, the work presented is much too esoteric to be of value. However, in 20 years, physicians may be dealing day-to-day with the problems of controlling multigenic diseases. No one knows how fast this field

can proceed. There is high probability that the answer to many familial disorders lies in a multigenic analysis. The practicing physician may get some understanding of the direction this field might take by reading the editorial, "Histocompatibility antigens, immune responsiveness and susceptibility to disease" by McDevitt and Bodmer which appeared in the January, 1972 issue of the *American Journal of Medicine*.

PHILLIP PERIMAN, M.D.

The Drug Abuse Controversy. CLINTON C. BROWN, Ph.D. AND CHARLES SAVAGE, M.D., Editors. Price, \$8.50. Pp. 270. Baltimore, Maryland: Friends Medical Research Center, Inc. National Educational Consultants, 1971.

The book is based on a 1970 Symposium on the subject participated in by professionals and laymen.

Opinions ranged from "freedom of self-medication" as a "fundamental right" (Thomas S. Szasz, M.D., libertarian psychiatrist), to "the law really is the cause of the drug controversy" (John A. Robertson, Esq., lawyer), to anticipating public acceptance of wider legitimate, including self-actualizing, potentialities of the subject substances (Jean Houston, Ph.D., psychologist).

Neil Solomon, M.D., Ph.D., Secretary of Health and Mental Hygiene, State of Maryland, set the tone of the meeting in advocating more research, questioning the effectiveness of educational efforts, and bemoaning "the low percentages of 'cures'".

Marihuana, he stated, is only psychologically, not physically, habituating. In 1973 he could have added that the much-delayed research is showing few, if any chronic effects, and some possibly beneficial therapeutic effects, such as bronchodilation and perhaps lowering of ocular tension by marihuana.

In a society in which disregard for the law, and overindulgence in medications, alcohol, and tobacco among adults are rife, communication with young drug abusers naturally fails on the basis of precepts and even facts.

Even the representative of the Bureau of Narcotics and Dangerous Drugs, the present Drug Enforcement Agency, admitted that "laws don't change a thing but human beings do".

BOOK REVIEWS

Methodism with its new values cured the gin epidemic in London of the 18th century as Daniel Fieldman, M.D., psychiatrist, pointed out. Provision of viable alternatives, such as coffee and beer houses, also helped.

It is hard to accept the law monopoly (J. A. Robertson) or the doctor monopoly (T. S. Szasz) as the bases of drug abuse.

"Is turning on with drugs any different from greed in eating, drinking, accumulating worldly goods and empire building as escape into boredom from true human needs and fulfilments?" the young ask. "The drug solution has already become a technological Trojan horse" (H. Lennard).

Methadone treatment of heroin addicts produced a more docile addict, but, admittedly, not a healthy person in a healthy social milieu (O. Lee McCabe, Ph.D., psychologist).

L. Yablonsky, Ph.D., sociologist, discussed such an artificial socializing milieu, the Synanon Society of ex-addicts. Some dependence remains, but on a much more mature level.

Psychedelic psychotherapy (C. Savage, M.D. and O. L. McCabe, Ph.D.) fights fire with fire. However, psychedelic "highs" have more religious ("binding together") than therapeutic significance.

Of the solutions proposed, repeal of restrictive laws must yield to restricted production and supply, 92% so far in the case of anorectic agents. This has certainly limited their overuse. Individual responsibility (T. S. Szasz) and social responsibility and rehabilitation are important parts of the answer. We must not stop with palliatives (methadone, etc.).

How do we promote "a sound mind in a sound body" (J. Locke)? By individual and social understanding, opportunity, and exercised values worthy of the advances in the sciences and the arts and of mature humanity.

Appendices on Society and Drugs, Students and Drugs, Public Law 91-513 (the Comprehensive Drug Abuse Prevention and Control Act of 1970), and 113 references follow the individual presentations of views by the 20 experts.

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ECG PROBLEMS

(from page 150)

INTERPRETATION: Tracing 1: Left bundle branch block.

The QRS contours show typical left bundle branch block. The ST-T contours are consistent with this block, though digitalis effect or myocardial ischemia could be exaggerating them.

- Tracing 2:
1. Right bundle branch block.
 2. Left axis shift (left anterior hemiblock).
 3. First degree A-V block.
 4. Acute inferior wall and septal myocardial infarction.

Evidence of acute infarction is manifested by the loss of R wave in leads III and AVF, decrease in R wave amplitude in lead II, appearance of Q wave in lead V_2 , and dramatic change in ST-T contour in lead III. The shift from left to right bundle branch block and the sudden appearance of first degree A-V block (PR 0.24 seconds) is dramatic. Evidently, the patient had complete block of the left anterior fascicle. At the time the first tracing was taken, the left posterior division was partially blocked, but the right bundle branch was conducting normally. This allowed the impulse to enter the ventricles along the right bundle branch and activate the left ventricle across the right bundle branch and activate the left ventricle across the septum. However, when she developed fresh infarction, the right bundle branch became blocked. The posterior division of the left bundle still was only partially blocked, hence the impulse entered the ventricles along that division. Its partial blockade is shown in the prolonged PR interval. It was conducting, but slowly.

This is an instance of nearly complete trifascicular block. There is no conduction across the right bundle branch or the anterior division of the left bundle branch. Conduction across the posterior division is impaired. If it becomes any worse, there will be no A-V conduction. This situation did develop during the insertion of a temporary pacemaker with the development of complete A-V block and the resulting ventricular rate of 35 per minute.

*Edited by
Robert R. Montgomery, M.D.*

THE VIEW BOX

(from page 110)

DIAGNOSIS: Homozygous Sickel Cell Anemia

The radiograph showed destructive and productive osteitis of multiple phalanges and metacarpals. *SALMONELLA TYPHIMURIUM* was cultured. The differential diagnosis of dactylitis in a child includes tuberculosis, lues, and sickle cell anemia. This may take the form of either a sterile infarct or of an osteomyelitis, usually of a salmonella organism as in this case.

Todd D. Clopper, M. D.
Chief Resident
Department of Radiology
Washington Hospital Center

*Edited by Gunther J. Augustin, M.D.
Senior Attending Radiologist, Washington
Hospital Center, Washington, D.C.*

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Use generic or descriptive names of drugs when available. Trade names, capitalized, may be given in parentheses when the drug is first mentioned.

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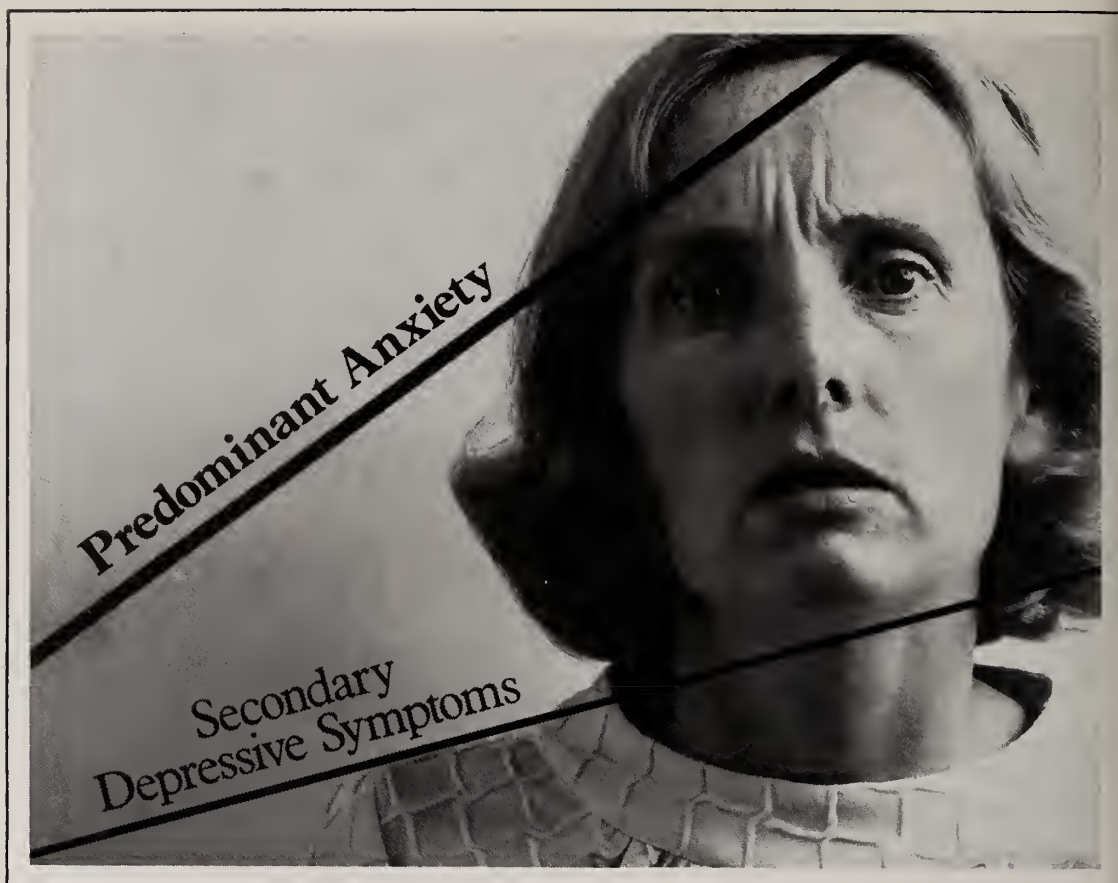
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INTERACTIONAL BEHAVIOR IN
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**The
latest news
in weight
control is
still the good,
balanced diet—
but less.**

Perhaps two-thirds of our people should go to bed hungry every night." The nutritionist who made this statement recently was not being inhumane. Rather, he was suggesting that many Americans would do well to deprive themselves of such institutions as the second helping and the midnight snack.

For many overweight persons the answer is not a "crash" program but a "crack-down" on the quantity and quality of food eaten. Sound advice for dieters remains: Follow a good, balanced diet and wage war against bad eating habits. To lose weight, eat less.

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CONTENTS

SCIENTIFIC ARTICLES

Opiate "Overdose" Deaths in the District of Columbia. I. Heroin-Related Fatalities. Mark H. Greene, M.D., James L. Luke, M.D. and Robert L. Dupont, M.D.	175
Interactional Behavior in An Alcoholic Community. Steven J. Wolin, M.D., and Peter Steinglass, M.D.	183
Colonoscopy—Fiberoptic Endoscopic Approach to the Colon and Polypectomy. David C. Wherry, M.D. and Harry Zehner, Jr., M.D.	189
Intraventricular Hematoma Successfully Treated by Surgery. Spiros Koulouris, M.D., Nasrollah Fatehi, M.D. and F. Donald Cooney, M.D.	193
Multiple Excavating Pulmonary Metastases. David Simon, M.D.	197

OTHER FEATURES

President's Message On Giving. Clifton Gruver, M.D.	5
Editorial Medical Records. Alfred Baer, M.D.	6
Scientific Editorial Anticoagulation II: Anticoagulant Usage in Cerebrovascular Disease. Richard Edelson, M.D.	7
Post Graduate Education Medical Management of Rheumatoid Arthritis. Anthony J. Sliwinski, M.D.	217
The View Box Edited by Gunther J. Augustin, M.D.	182
ECG Problems Edited by Robert R. Montgomery, M.D.	188
Book Reviews Pharmacology-Drug Actions and Reactions. (Levine) Reviewed by Richard Gillis, Ph.D. Malnutrition—Its Causation and Control. (Robson) Reviewed by James M. Moss, M.D. Neuro-Ophthalmology. (Smith and Glaser) Reviewed by David K. Berler, M.D. Hamilton Bailey's Demonstrations of Physical Signs in Clinical Surgery. (Crain) Reviewed by Harry Zehner, Jr., M.D.	223
Information for Authors	229
Advertising and Subscription Information	232
Index to Advertisers	232

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PRESIDENT'S MESSAGE

ON GIVING

Do you donate blood? I don't—except once in a blue moon. I forget, or I'm too busy, or it's an inconvenient location or time, or I just don't think about it.

We could do better as a professional group, and should—particularly when we utilize blood on a day-by-day basis, appreciate the need, and see its life-supporting results.

I think we are also missing another good bet when it comes to procurement. Who could more effectively convince the public to donate blood than the personal physician? I seldom remember to suggest it to my patients—do you?

To *improve supply*, we must *think* blood—just as we *think* Pap smears, breast exams, proctoscopies, annual physicals, immunization, and all those things that have become routine in our admonitions to our patients.

Conserve the blood supply we do have. When you order blood, try to see that it is replaced. Tell your patient, the family, visiting friends, etc., of the need for their involvement in this.

And *utilize* it preciousely. Every transfusions should meet absolute indications—might your patient have managed adequately on four units, instead of the five actually received?

These are some of the things we can do as individual physicians to help our blood programs.

The Medical Society, as an organization, can likewise conduct educational campaigns, as during National Blood Donor Week, or at other times via the news media, with efforts of our Committee on Public Information and Education, our Speakers Bureau, and the liaison we enjoy with other large professional, business, and civic organizations.

The American Red Cross Washington Regional Blood Center supplies the majority of blood and blood products for local use. It also supplies a larger, regional district in addition to the District of Columbia. The ARC Regional Center has liaison with the Medical Society of the District of Columbia primarily through our Committee on Blood and Tissue Transplants. Occasionally, representatives from neighboring medical jurisdictions have met with that Committee and the ARC consultants, but such meetings have been sporadic.

It is generally agreed to be in the national interest to enlarge and improve blood banking services. Congress and the executive arm of our government have voiced views on such a need. Time is ripe for developing a true National Blood Program. Legislation is in the hopper designed to achieve this. The AMA supports it. Close liaison between blood providers and blood users is necessary—regional cooperation is imperative. The MSDC hopes to catalyse such efforts.

Regardless of what organizational improvements evolve, adequate supply and utilization (donor and recipient) demand your personal and individual attention. Let's make a continuing extra effort for this vital cause.

CLIFTON R. GRUVER, M.D.
PRESIDENT



Clif Gruver

DR. CLIFTON GRUVER

Editorial

Medical Records

Medical records are repositories of valuable information which is being abused these days in many subtle ways.

When a patient applies for life insurance, he is usually asked to sign a release requesting his physician to furnish the insurance company all of the health information in his possession. If the patient had the wisdom to submit to the searching physical examination offered nowadays to the health-minded, the doctor probably uncovered some minor abnormality: a tiny asymptomatic fibroid; a minimally enlarged inguinal ring; a marginally elevated uric acid; a random hypertensive reading never again confirmed. When furnished to an insurance company, reports of these findings are not read in the spirit in which they are written. A quasicosmetic defect, conveyed to the patient with words of reassurance, and to the chart with a reminder to re-check later, is now transformed into ammunition to either deny the application or to accept it at increased rates. Rumor has it that such data are fed into computer banks available to other companies, forever to haunt the applicant like a

criminal record from which there is no presidential pardon. The patient receives a cryptic letter from the insurer leaving him bewildered and irate—against his doctor. There is a tear in the delicate fabric of the doctor-patient relationship with bitterness on both sides, the patient wishing he had left well enough alone, and the doctor regretting that he had been so thorough.

Unlike the very proper and necessary health insurance claim form, the private physician's report to a life insurance company is a very inexpensive means for a profit-making concern to screen its risks. I submit that a doctor is not acting in his patient's best interests when he makes records available in this manner. Rather, the insurer should be the one to determine the applicant's eligibility, making use of information obtained from the latter himself, and from an examination performed by a physician on its payroll who leaves no doubt as to which master he serves. Only if an abnormality turns up during this investigation, should the insurer request relevant background information from the personal doctor. The reply to such an inquiry would be specific and to the point—not the abundant haul of a fishing expedition.

ALFRED BAER, M.D.



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SCIENTIFIC Editorial

ANTICOAGULATION II: Anticoagulant Usage in Cerebrovascular Disease

Richard Edelson, M.D.

In the last two decades a large clinical experience, including well organized studies, has clarified the general guide lines for the use of anticoagulants (primarily coumarin derivatives and heparin) in cerebrovascular disease (CVD). While the therapeutic role of anticoagulant therapy in CVD is much smaller than was initially expected, its use has strongly stimulated the study of the natural history of stroke.

The use of categorical terms is mandatory in discussing the use of anticoagulants in treating occlusive CVD. The current delineations are as follows: 1) transient ischemic attack (TIA), which is defined as an episode of focal neurological symptoms, with abrupt onset and rapid resolution lasting less than 24 hours and attributed to an alteration of the circulation to a limited region of the brain; 2) a progressing stroke, or thrombosis-in-evolution, in which there is a worsening of the neurological deficit over hours or days, which seems to be still progressing at the time the patient is evaluated; 3) a completed thrombosis where the focal neurologic deficit is stable; 4) acute embolic cerebral infarction in which the patient usually has rheumatic heart disease and fibrillation or a prosthetic heart valve. The primary objective of anticoagulant therapy is to impede or prevent thromboses and thus maintain the integrity of arterial flow patterns, and, in certain instances, to prevent the formation of emboli which consist of fragments of thrombus.

Twenty-five to forty per cent of patients who have more than one TIA will have a cerebral infarction if followed for five years.¹ A large proportion of these infarcts will occur within the first few months after the first TIA. Numerous studies have demonstrated a striking reduction in the incidence of TIAs and of subsequent cerebral infarctions of patients receiving anticoagulants.^{2,3} However, anticoagulants have not been shown to significantly alter the mortality in treated versus untreated groups, probably because the primary cause of death in patients with CVD is cardiac disease.⁴ Recent data would suggest that most of the effect of anticoagulant therapy can be expected to occur in the first two months following the onset of a TIA.⁵ This is consistent with the concept that an ulcerated atheromatous lesion in an artery leading to the brain, thought to be the most

common lesion responsible for TIAs, is not static but undergoes changes, so that it shreds embolic fragments most readily during the early stages of the disease. If this is the case, then anticoagulant therapy is likely to be of most value in regard to prevention of microembolization in the first few weeks after symptoms are manifest.

The problem in the application of anticoagulant therapy to thrombosis-in-evolution is to distinguish at any given point in time between the patient whose lesion is going to progress and one whose deficit has reached its maximum. Several small studies have shown that anticoagulants are beneficial as regards the degree of neurologic deficit and case fatality in patients with a progressing stroke.^{6,7} Since it is difficult to assess thrombosis-in-evolution and since it is often difficult to monitor these patients from hour to hour by trained personnel, I have often used short-term heparinization in patients who present acutely with a mild stroke and who are in other respects good candidates for anticoagulation.

Anticoagulants have been shown to be of no benefit in the rate of degree of recovery in completed cerebral infarcts and they fail to afford protection against recurrent cerebral infarctions.^{8,9}

The rationale for the use of anticoagulants in acute embolic cerebral infarction is to reduce the chance of subsequent embolism. Often after one incident showers of emboli follow. The general consensus of the literature is that the frequency of recurrent emboli and overall mortality in patients with cerebral emboli are reduced by anticoagulants. A controversy has arisen as to when to give anticoagulants following a cerebral embolus. Some experimental work would indicate that anticoagulant therapy may increase the risk of intracerebral hemorrhagic complications after acute cerebral embolism.¹⁰ Though some authors would recommend waiting three weeks before anticoagulating, a significant number of recurrent cerebral emboli will occur within the first few weeks after the initial episode. A good compromise appears to be the practice of Douglas, who uses oral anticoagulant drugs and not heparin so that there is an interval of 36-48 hours before an anticoagulant effect is established.¹¹

The contraindications of anticoagulant usage include poor patient cooperation, chronic alcoholism,

peptic ulcer disease, intensive salicylate therapy, malignant hypertension, hepatic disease, subacute bacterial endocarditis, recent surgery or trauma to the central nervous system, uremia and any patient with a pre-existing hemostatic defect. Lumbar punctures should always be done prior to anticoagulation to rule out cerebral hemorrhage.

It is important to realize that the stroke population is older than the coronary group. Not only is the risk of bleeding on anticoagulants higher in the elderly but also the stroke patient often does not think as clearly and at times it is likely to be ataxic and fall. Thorough supervision is essential in anticoagulating the patient with CVD.

Recently aspirin because of its antiplatelet aggregation effect has been utilized in the treatment of TIAs. Its use is based on the findings which suggest that fibrinplatelet emboli may be a major contribution to TIAs. A dose of 600 mg. per day is used and the side effects are less. Several case reports as well as one retrospective study have shown a decline in the incidence of subsequent TIAs; however, a difference in the rates of infarction and death has not as yet been demonstrated.^{1,3,14,15}

1. MILLIKAN, C.H.: Reassessment of anticoagulant therapy in various types of occlusive cerebrovascular disease, *Stroke* 2:201-108, 1971.
2. SIEKERT, R.G., WHISNANT, J.P., MILLIKAN, C.H.: Surgical and anticoagulant therapy of occlusive cerebrovascular disease. *Ann. Int. Med.* 58:637-641, 1963.
3. BAKER, R.N., et al: Anticoagulant therapy in cerebral infarction: Report in cooperative study. *Neurology* 12:823-835, 1962.
4. WHISNANT, J.P., MATSUMOTO, N., ELVEBACK, L.R.: Transient cerebral ischemic attacks in a community: Rochester, Minnesota, 1955 through 1969. *Mayo Clin. Proc.* 48:194-198, 1973.
5. WHISNANT, J.P., MATSUMOTO, N., ELVEBACK, L.R.: The effect of anticoagulant therapy on the prognosis of patients with transient cerebral ischemic attacks in a community: Rochester, Minnesota 1955 through 1969. *Mayo Clin. Proc.* 48:844-848, 1973.
6. CARTER, A.B.: Anticoagulant treatment in progressing stroke. *Brit. Med. J.* 2:70-73, 1961.
7. FISHER, C.M.: The use of anticoagulants in cerebral thrombosis. *Neurology* 8:311-332, 1958.

8. MARSHALL, J., SHAW, D.A.: Anticoagulant therapy in acute cerebrovascular accidents: A controlled trial. *Lancet* 1:995-998, 1960.
9. HILL, A.B., MARSHALL, J., SHAW, D.A.: Cerebrovascular disease. Trial of long-term anticoagulant therapy. *Brit. Med. J.* 2:1003-1006, 1962.
10. WOOD, M.W., et al: Relationship between anticoagulants and hemorrhagic cerebral infarction in experimental animals. *Arch. Neurol. Psychiat.* 79:390-396, 1958.
11. DOUGLAS, A.S.: Management of thrombotic diseases. *Seminars in Hematology* 8:95-139, 1971.
12. Aspirin, Platelets, and Stroke. Edited by Fields, W.S. and Hass, W.K. St. Louis, W.H. Green, 1971.
13. MUNDALL, J. et al: Transient monocular blindness and increased platelet aggregability treated with aspirin. *Neurology* 22:280-285, 1972.
14. HARRISON, M.J.G., et al: Effect of aspirin on aneurysm fugax, *Lancet* 2:743-744, 1971.
15. DYKEN, M.L., KOLAR, O.J., JONES, F.H.: Differences in the occurrence of carotid transient ischemic attacks associated with antiplatelet aggregation therapy. *Stroke* 4:732-736, 1973.

Before prescribing, see complete prescribing information in SK&F literature or PDR. The following is a brief summary.

Indications: Edema associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. Also, mild to moderate hypertension.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (> 5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently — both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Anti-hypertensive effects may be enhanced in post-sympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Rarely, necrotizing vasculitis, paresthesias, icterus, pancreatitis, and xanthopsia have occurred with thiazides alone.

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The National Wholesale Druggists'
Association



Joint Statement on Antisubstitution Laws and Regulations

The purpose of this statement is to affirm the support of the participating organizations for the laws, regulations and professional traditions which prohibit the unauthorized substitution of drug products.

Traditionally, physicians, dentists and pharmacists have worked cooperatively to serve the best interests of patients. Productive cooperation has been achieved through mutual respect as well as a common concern for the ideals of public service. This mutual respect has been reflected, in part, by joint support over the years for the adoption and enforcement of laws and regulations specifically prohibiting unauthorized substitution and encouraging joint discussion and selection of the source of supply of drug products. The basic principles of medical, dental and pharmacy practice are thus utilized and preserved in the interest of patient welfare.

The antisubstitution laws have not obstructed enhancement of the professional status of pharmacy any more than they have in and of themselves guaranteed absolute protection from unsafe drugs, or freed physicians, dentists and pharmacists from their responsibilities to patients. As a practical matter, however, such laws and regulations encourage interprofessional communications regarding drug product selection and assure each profession the opportunity to exercise fully its expertise in drug usage, to the advantage of patients.

Physicians and dentists should be urged to increase the frequency and regularity of their contacts with pharmacists in selection of quality drug products, recognizing that

economies to patients can be improved through such communication, taking into account the patients' needs. The pharmacist's knowledge of the chemical characteristics of drugs, their mode of action, toxic properties and other characteristics that assist in making drug selection decisions should be utilized to the fullest extent practicable by physicians and dentists in serving their patients.

Since drug product selection entails knowledge derived from clinical experience, the physician's and dentist's roles in product selection remain primary and do not permit delegation of decisions requiring medical and dental judgments. A broader role in therapy will evolve for pharmacists as improved understanding and cooperation among the professions continue to grow.

There has been no evidence that there are convincing reasons to modify or repeal existing laws and regulations prohibiting the unauthorized substitution of another drug product for the one specified by a prescriber. It is our belief that such laws and regulations merit the joint support of the medical, dental and pharmaceutical professions and the pharmaceutical industry.

Add your opinion to the weight of other professionals and send it to your state assemblyman or legislator.

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SCIENTIFIC ARTICLES

Opiate "Overdose" Deaths in the District of Columbia I. Heroin-Related Fatalities

MARK H. GREENE, M.D., JAMES L. LUKE, M.D. AND ROBERT L. DUPONT, M.D.

Abstract

Between July 1971 and December 1972, there were 118 acute opiate overdose fatalities in the District of Columbia, 58 of which resulted from heroin abuse. Analysis of these cases suggested that the lethal effect of heroin was dose related (i.e., a toxic effect). Lack of opiate tolerance, documented in 51% of the cases, contributed significantly to mortality. Possible synergy between heroin and alcohol was suggested by higher proportions of alcohol positives among heroin overdose victims when compared to controls ($p < .05$). Quinine and other adulterants probably did not contribute to a fatal outcome among users of street heroin. The validity of a mysterious "sudden death syndrome" following parenteral heroin abuse is doubtful in view of the data presented.

Introduction

The fundamental epidemiological aspects of acute heroin fatalities have been well described^{1,2}. However, a clear understanding of the pharmacophysiological factors which produce death following the abuse of a street opiate drug has not been reached. This situation was emphasized recently by Brecher³, who argued that most deaths labelled as opiate "overdoses"

could not be explained simply on the basis of the traditional pharmacological consequences of excessive concentrations of heroin and/or methadone on the central nervous system. The protective effect of well established opiate tolerance in blunting the action of larger-than-normal doses of heroin has been demonstrated in addicts using heroin regularly⁴, and in addicts maintained on methadone for therapeutic purposes⁵.

These studies make it difficult to understand how persons regularly using either heroin or methadone could die from an "overdose" of these opiates in the amounts usually administered. A further conceptual complication is the syndrome of sudden death purported to occur within minutes following an intravenous injection of street heroin. Deaths of the latter type appear to occur much too rapidly to invoke incremental central nervous system depression as the mechanism of death^{1-3,6,7}. Consequently, the term "overdose" has served to indicate lack of understanding of the true mechanism of death in fatalities directly related to opiate abuse.

This study presents an analysis of a cohort of carefully investigated, consecutive, acute opiate fatalities, in order to better understand those factors that may have contributed to a

This study presents an analysis of a cohort of carefully investigated, consecutive, acute opiate fatalities, in order to better understand those factors that may have contributed to a fatal outcome.

fatal outcome. None of the deaths reported in this series were included in the previous report from the District of Columbia⁸. Deaths directly related to heroin abuse are detailed in this paper. Methadone-related fatalities will be reported in a separate publication.*

Materials and Methods

In July, 1971, Washington, D.C., converted to a Medical Examiner System for medical-legal death investigation. Since that time, there has been uniform, systematic investigation of sudden, unexpected and/or medically unattended deaths in the District of Columbia, including all known or

OPIATE "OVERDOSE" DEATHS IN THE DISTRICT OF COLUMBIA

GREENE, LUKE AND DUPONT

suspected narcotic-related fatalities. Investigation of drug-related deaths is supported by a modern, comprehensive on-site toxicology capability.

All deaths directly related to opiate abuse identified from July, 1971, through December, 1972, form the basis of this report. There were 118 heroin and/or methadone "overdose" deaths investigated during the study period. All such cases were subjected to complete postmortem and toxicological examination. Marked pulmonary edema and hyperplasia of the lymph nodes of the porta hepatis constituted the only significant pathological abnormalities.

Excluded from the study group were deaths resulting from the various recognized medical complications of narcotism (sepsis, bacterial endocarditis, tetanus, viral hepatitis, etc.) and unnatural deaths among users of narcotic drugs. Also excluded were those addicted persons who were found to have died from natural causes. Generically, the study group was found to be comprised primarily of young, black, inner-city males with a history of acute and/or chronic opiate abuse, and with the cutaneous stigmata of acute and/or chronic narcotism. Positive morphine/quinine toxicology was obtained in 98% of cases.

The case records of the study group were examined retrospectively and data were analyzed summarizing specific demographic variables, death scene investigative findings, the circumstances surrounding death, post-mortem pathology and toxicological results.

A control group consisting of 75 homicidal fatalities among opiate users during the same study period was analyzed in similar fashion.

The 58 heroin "overdose" fatalities identified during the study period form the basis of this paper.

In an effort to characterize the various components of the addict

study and control group populations in terms of longevity of opiate usage, current tolerance status, and route of opiate administration, certain assumptions were necessarily made. While these considerations are admittedly somewhat arbitrary, they were applied equally to both the study and control groups in random fashion and without knowledge of the particular circumstances of death prior to tabulation.

A decedent was considered to have been opiate addicted in the past if the cutaneous stigmata of chronic intravenous narcotism were present or if a positive history of regular opiate use was elicited during the death investigation. A decedent was considered to have been addicted at the time of death if there was a clear history of regular heroin use immediately prior to death in conjunction with fresh venipuncture site(s) and if there was no historical evidence suggesting a recent period of opiate abstinence (incarceration, hospitalization) in the two months prior to death. Those classified as active addicts at the time of death were characterized as having opiate tolerance; those who were not known to have been using heroin regularly at the time of death were considered to lack opiate tolerance.

If a fresh venipuncture site was found at autopsy, and toxicological analysis of stomach contents was negative, the route of opiate administration was considered to be intravenous. If no fresh venipuncture was found, and stomach content toxicology was positive, the route was considered oral. If both a fresh venipuncture site and positive stomach toxicology were present, the route was considered both intravenous and oral. If neither were present, the route was characterized as indeterminate.

Since tissue drug levels are a function of dose, route of administration, time elapsed between drug administration and death and many other factors, we decided to concen-

trate simply on the presence or absence of a particular drug(s) in analyzing toxicological results. An exception was made in this regard for blood morphine levels⁹. Based on observations made on the rate of clearance of intravenous blood morphine in man¹⁰, we elected to divide the heroin fatalities into three toxicological subgroups: blood morphine ≥ 0.03 $\mu\text{gm/ml.}$, blood morphine < 0.3 $\mu\text{gm/ml.}$, and blood morphine not determined. Blood ethanol levels of less than 20 mgs/100 ml were not considered positive.

If methadone alone was recovered toxicologically, the death was classified as a methadone death. A heroin death was defined as a case toxicologically positive for morphine and/or quinine. (Unpublished laboratory data here indicates that cases found to be positive for quinine alone connote heroin administration in which blood and/or urine morphine levels are too low for detection by standard photofluorimetric and other analytical techniques.) Cases in which both heroin and methadone were detected were classified as combination deaths.

Accurate indices of street heroin quality and availability are developed in Washington, D.C., on a regular basis¹¹, and are summarized monthly. Such data permit on-going monitoring of the average number of milligrams of heroin in a street level package.

Results were analyzed for statistical significance using the Student "t" test, Chi square and the Pearson Correlation Coefficient. Trends were demonstrated using a linear regression line fit by the method of least square.

Results

A. General

During the study period, there were 118 acute opiate "overdose" deaths of all types, 58 of which were attributed to heroin alone, 39 to methadone

alone and 21 to the combination of both heroin and methadone (see Fig. 1).

Demographic parameters of the heroin "overdose" sub-group are presented in Table I and are quite similar to those that have been published elsewhere^{1,2}. In addition, the heroin "overdose" victims as a group were significantly older than those who were classified as methadone or combination fatalities ($t = 3.14$, $p < .01$). There was a marked shift in relative proportion of toxicity from heroin predominant during the first six months of the study to methadone, predominant in the last six months (see Fig. 1). Geographically, the heroin overdose victims lived in the same census tracts which had the highest clinical addiction rates ($r = 0.600$, $p < .01$).

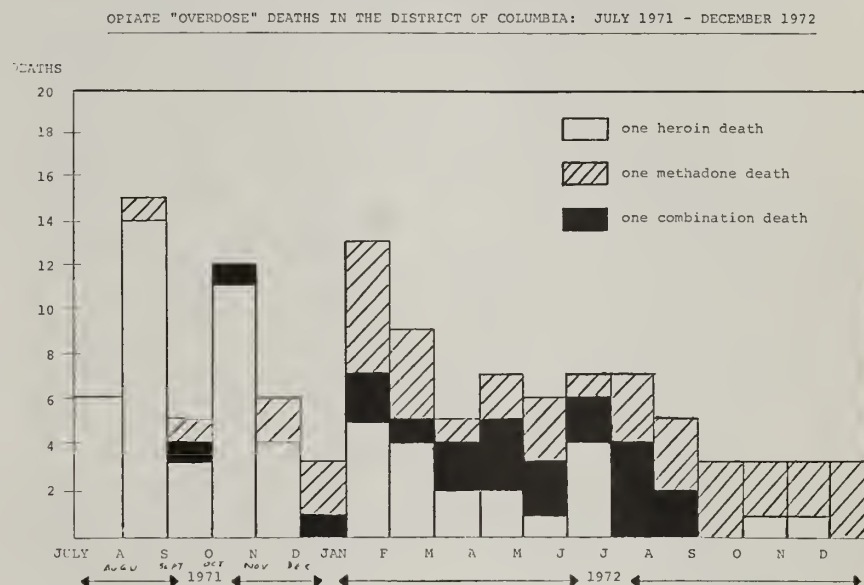
The control group was identical to the total opiate overdose group with respect to all demographic and pathological variables tested except lung weight (see Table I).

B. Route of Administration

Heroin was virtually always administered by the intravenous route. In the 53 cases in which this determination could be made, 100% had a fresh venipuncture site(s) and negative stomach content.

C. Addiction/Tolerance Status

Only 13.8% of all heroin "overdose" deaths occurred among decedents who had not been addicts at some point in their lives. However, a much larger percentage (51.1%) were not known to have been addicted at the time of their death. The latter are decedents in whom lack of opiate tolerance may have contributed to death. Roughly, one quarter of those who lacked tolerance had never been addicts, and the remainder were addicts who had recently become



abstinent by history. It should be noted that this is almost certainly an underestimation of the number of decedents who lacked opiate tolerance at death. In addition, the presumable tolerant group certainly includes persons for whom the required history of abstinence could not be elicited, but who were in fact abstinent. It also may include individuals who used heroin intermittently but who were considered regular users by history.

D. Pulmonary Edema

Severe pulmonary edema is said to be a characteristic postmortem finding among opiate overdose victims^{1,2}. Comparison of lungs weights between the study group (mean = 1293.1 gms.) and the control group (mean = 914.4 gms.) verifies this observation ($t = 7.1179$; $p < .001$). There was no significant difference in lung weight between heroin, methadone and combination death victims.

E. Presence of a Second (non-opiate) Drug

In 32 (55.2%) of the heroin "overdose" victims and 36 (48.0%) of the controls, a non-opiate drug was identified by toxicological analysis (see Table II). Ethanol was much more likely to be identified in association with cases classified as heroin fatalities than with either methadone or combination deaths ($X^2 = 11.6590$, $p < .01$, $df = 2$). In addition, heroin "overdose" victims had a significantly higher rate of ethanol positivity than the control group ($X^2 = 4.2700$, $p < .05$). The relative lack of amphetamine positive toxicologic studies among heroin decedents may reflect statistical artifact created by the declining heroin overdose death rate during the summer of 1972, when amphetamine abuse was widespread in Washington^{1,2}.

OPIATE "OVERDOSE" DEATHS IN THE DISTRICT OF COLUMBIA

GREENE, LUKE AND DUPONT

TABLE I: Data Comparing Opiate Fatalities with Heroin Victims and Control Population

Category	Opiate Deaths		Heroin Deaths		Control Group	
	# of cases	% of total	# of cases	% of total	# of cases	% of total
Number of cases	118		58		75	
Age (mean years)	24.7		27.1		26.3	
Sex						
male	99	83.9	49	84.5	70	93.3
female	19	16.1	9	15.5	5	6.7
Race						
black	114	96.6	58	100.0	72	96.0
white	4	3.4	0	—	3	4.0
Marital status						
single	75	63.6	37	63.8	53	70.7
married	33	28.0	16	27.6	17	22.7
other	10	8.4	5	8.6	5	6.6
Employed						
yes	63	53.4	33	56.9	41	54.7
no	53	44.9	23	39.6	32	42.7
unknown	2	1.7	2	3.5	2	2.6
Fatty liver	23	19.5	11	19.0	11	14.7
Hyperplastic portal lymph nodes	48	40.8	21	36.2	28	37.3
Chronic needle tracks	73	61.9	38	65.5	64	85.3
Ethanol positive	44	37.3	30	51.7	24	32.0
Lung weights (mean grams)	1293.1		1284.8		914.4	

F. The Role of Quinine

Street heroin available on the East Coast in general, and in the District of Columbia in particular, is customarily adulterated with quinine. This had led to speculation that an adverse reaction to quinine may be responsible for the sudden death syndrome among heroin addicts. Unfortunately, our data does not allow us to reach a definitive conclusion in this regard. All of the sudden death sub-group cases were positive for quinine, as were 80% of heroin and combination "overdose" deaths and 84% of heroin and combination positive homicide victims. The number of decedents positive for quinine alone was too small to permit statistical analysis.

G. The Sudden Death Syndrome

Given the rapidity with which intravenous morphine is cleared from the blood¹⁰, we hypothesized that finding an elevated blood morphine

TABLE II: Non-Opiate Drugs Detected by Toxicological Analysis in the Tissues of Heroin Victims and Addict/Homicide Control Population

Drug(s) Identified	Heroin Deaths	Control Group
Ethanol only	28	19
Ethanol + another drug	2 ¹	5 ²
Other depressant drug only	1 ³	0
C.N.S. stimulant only	1 ⁵	12 ⁴
Total	32	36

¹ One propoxyphene, one barbiturate.² Five amphetamine.³ One chlorpromazine.⁴ Ten amphetamine, one cocaine, one phenmetrazine.⁵ One salicylate.

level (≥ 0.3 $\mu\text{gm/ml.}$) might identify decedents who had died rapidly (i.e., within 15 minutes of injection). Thirty-three heroin "overdose" fatalities and 23 control cases had blood morphine determinations performed. Of the control group, 20 had blood morphine levels that were undetectable, two had trace positive determinations (.04 and .03 $\mu\text{gm/ml.}$) and one (4.3%) had an elevated level (0.33 $\mu\text{gm/ml.}$). In contrast, five of the heroin "overdose" victims had undetectable levels, 14 had low levels (mean 0.13 $\mu\text{gm/ml.}$), and 14 had elevated levels (mean 0.53 $\mu\text{gm/ml.}$). Comparison of the 14 elevated level cases with the 19 cases with low to undetectable blood morphine levels failed to reveal any significant demographic, pathologic, historic or other toxicological differences.

H. Coexisting Hepatic and Renal Disease

Both the liver and kidney play important roles in opiate metabolism

and excretion¹³. Functional impairment of either organ system might potentiate the pharmacological effects of opiates, thereby enhancing drug morbidity and mortality. However, similar rates of hepatic and/or renal pathology were found in the study and control groups.

Discussion

Opiate "overdose" victims constitute a remarkably homogeneous group of cases in terms of their demography but are heterogeneous relative to those factors that might have contributed to death.

Heroin deaths in the District of Columbia occur following intravenous administration of a heroin/quinine mixture and may occur quite suddenly, within minutes following drug administration. Amphetamine use was never observed in this group, whereas ethanol use was very common. A minority of heroin deaths seemed to occur in a more prolonged fashion, with progressive central nervous system depression resulting in cardiopulmonary arrest. Heroin deaths tended to occur among an older population of addicts and declined dramatically in number over the last six study months.**

Death from "morphine poisoning" is said to be a gradual process¹⁴. However, a substantial proportion of heroin deaths appear to occur too rapidly to invoke incremental central nervous system depression as a reasonable pharmacophysiological mechanism. In addition, the range of opiate dosage lethal for heroin addicts reported in the literature ranges from 200 mgs.¹⁵, to 500 mgs.¹⁶, far in excess of the street dose administered during the study period¹¹. In addition, it has been shown that sudden changes in heroin dosage administered to an addicted population (to nine times baseline level) failed to produce any adverse symptoms⁴. We, there-

fore, examined other factors that might have contributed to a fatal outcome.

To place this study in proper context, it should be noted that a severe, sustained scarcity of heroin developed in Washington, D.C., during the last eight study months¹¹. The number of police heroin purchases and seizures fell sharply during this interval. The potency of street heroin declined from an average of 6% in 1969 to 2% in the last quarter of 1972 while the per-milligram price of heroin rose fivefold. The average number of milligrams of pure heroin in street level packages declined from 16.4 (± 18.8) in February, 1972, to 3.0 (± 6.8) in December, 1972. The number of arrestee urines found to be toxicologically positive for heroin in the District of Columbia Superior Court drug surveillance facility also declined sharply¹¹.

As heroin became both scarce and expensive, the heroin "overdose" death rate declined proportionately and dramatically (see Fig. 1). There was a strong positive correlation between the absolute number of monthly heroin "overdose" deaths and the monthly average number of milligrams of heroin found in police street heroin purchases during the study period ($r = .8285$, $p < .01$). In addition, the per-package concentration of street heroin became more uniform, reducing the likelihood of a user obtaining a package of heroin with unexpectedly high concentration. These data strongly suggest, in contrast to the opinions cited previously³, that heroin does, in fact, play a direct, dose-related role in causing "overdose" deaths. Similar correlations have recently been developed in Atlanta, Georgia¹⁷.

Additional support for a direct, causative role for heroin, and against those theories which attempt to implicate quinine, other adulterants, or even a non-specific effect secondary

to an intravenous colloid bolus is articulated as follows: First, heroin "overdose" deaths occur in parts of the country where street heroin is not adulterated with quinine, i.e., on the West Coast. Second, consonant with the declining availability and quality of heroin in Washington, the injectable narcotic material has been found to contain relatively constant amounts of quinine.[†] Yet the heroin death rate has dropped dramatically, with only two heroin "overdose" fatalities occurring in the last six months of 1972. Finally, if quinine were a critical determinant in heroin-related deaths, one would not expect methadone to protect patients from the adverse effects of quinine or other adulterants used in processing heroin. Yet none of the heroin "overdose" cases reported here occurred in a patient receiving therapeutic methadone, during a period when some 10,000 addicted persons in Washington were being treated with methadone, some of whom continued to abuse heroin.

Although most of the decedents in this study had been heroin addicts at some time in the recent past, a surprisingly large percentage (51.1%) clearly lacked opiate tolerance at the time of death. This group was comprised of individuals who had been recently hospitalized, incarcerated or who were known not to have been using narcotics on a regular basis prior to their demise. An additional, unknown number probably lacked tolerance, but were classified as being tolerant because a definitive history of abstinence could not be elicited.

The protective value of opiate tolerance has been well demonstrated in studies among addicts using heroin regularly⁴ and among addicts on methadone maintenance⁵. Operationally, the protective effect has been documented by the absence of heroin deaths among patients on methadone maintenance in the District of Columbia during the study period. This is

OPIATE "OVERDOSE" DEATHS IN THE DISTRICT OF COLUMBIA

GREENE, LUKE AND DUPONT

somewhat surprising, considering that a substantial number of treatment patients are maintained on very low doses of methadone (26.5% of patients at, or below, 25 mgs. per day). Yet none of these individuals were found to have died from an opiate overdose while actively in treatment. In contrast to the literature, this would suggest that large doses of methadone may not be required to produce significant opiate tolerance^{5,18}. Therefore, lack of opiate tolerance may well potentiate opiate-related "overdose" fatalities. It should be noted that tolerance is a relative phenomenon. Patients on methadone maintenance have high tolerance relative to street level heroin, whereas the street addict may have relatively low tolerance. Such an explanation could well clarify why methadone patients can shoot heroin with impunity while street addicts still risk overdose.

The route of administration varies for different opiates. In this study, heroin was administered intravenously in almost all cases, whereas most of the methadone (particularly in the latter stages of the study) was taken by mouth. The sudden, physiologic impact of an intravenous bolus of heroin might be expected to produce lethal effects. On the other hand, it is unlikely that the intravenous administration of heroin can, by itself, account for the rapidity of some heroin deaths. Nearly one-third of intravenously administered heroin was associated with a prolonged (30 minutes or more) time course prior to demise. In addition, all of the controls took their heroin by vein and did not die from an "overdose." The intravenous route may be necessary, but it is not alone sufficient to cause the heroin sudden death syndrome.

A large group of decedents were found to have a non-opiate depressant drug in their systems (55.2%) with ethanol being by far the most common. The study group as a whole

was not significantly different from the control group in this regard. However, when heroin "overdose" fatalities were examined separately, a most provocative finding was noted. Heroin "overdoses" were more likely to be positive for ethanol than either methadone or combination "overdoses," or the control group (a statistically significant difference), raising the possibility that ethanol contributes in causative, and possibly synergistic fashion to these deaths.

Intravenous administered morphine is rapidly cleared from the bloodstream. In a group of non-addict volunteers given 10 mgs. of morphine (a dose similar to that injected by addicts in the District of Columbia during the study period), the highest blood morphine levels found 15 minutes following drug administration ranged from 0.1 - 0.2 $\mu\text{gms/ml}$.¹⁰. We hypothesized that the finding of a group of heroin "overdose" victims with substantially higher blood morphine levels ($\geq 0.3 \mu\text{gms/ml}$.) might identify those decedents who had died within minutes following heroin injection, representing cases of the so-called heroin sudden death syndrome. Of the 36 cases in which blood morphine determinations were performed, 14 (38.9%) had values in excess of 0.3 $\mu\text{gms/ml}$. Only one (4.3%) of the control cases fell into this range. Of the four victims found dead with the intravenous syringe still in their vein (a finding used in the past to substantiate the existence of the sudden death phenomenon), three (75%) fell into the elevated blood level category.

In eight of the 14 victims with elevated blood morphine levels, historical information was elicited documenting the elapsed time between drug administration and death. Of these latter cases, six (75%) had a history of death occurring within 15 minutes of drug administration. Of the 12 low blood morphine cases in which a similar determination could be made,

eight (66%) had a history of survival for 30 minutes or more following drug administration. These data suggest that cases with elevated blood levels may, in fact, connote examples of the heroin sudden death syndrome.

Variable blood morphine levels could possibly result from impaired heroin metabolism. However, similar rates of hepatic and renal disease between the high and low blood level groups suggest this not to be the case. Animal studies have shown that there is no real difference in the rate of morphine clearance from the blood between addicted and opiate-naïve animals¹⁹.

It is theoretically possible that an elevated dose of heroin eventuates in the sudden death phenomenon, and that lower doses are associated with the more classical syndrome of gradual central nervous system depression and death. No more than 40% of the heroin fatalities in this study could be examples of this syndrome, and it is likely that many fewer actually are.

Finally, it is possible that the heroin sudden death syndrome does not exist at all; the literature in this regard is more impressionistic than scientific. The duration between drug administration and death may well represent a synthesis of the quantity of heroin injected, the individual level of opiate tolerance, the rapidity of drug injection, the synchronous presence of other central nervous system depressant drugs, especially ethanol, and individual metabolic differences, the sum of which produces a broad range of rapidity over which death occurs.

Summary

The data here suggest that the lethal effect of heroin appears to be dose-related and that lack of opiate tolerance and the presence of ethanol contribute significantly to mortality among heroin addicts. Quinine and other adulterants probably do not

contribute to a fatal outcome among users of street heroin. As many as 40% of heroin fatalities may be examples of the sudden death syndrome. The specifics of each of the above considerations are discussed.

Addendum: Since submission of this paper, a report has been published which supports our contention that the effect of heroin is direct and dose-related in causing death from heroin overdose[‡]. To quote these authors: "The role of adulterants and hypersensitivity and other factors in the lethal episode was not evident. Such observations support the concept of a toxic mechanism of death, and the term 'overdose' is probably an appropriate one."

References

1. HELPERN, M., RHO, Y.: Deaths from Narcotism in New York City. *International Journal of the Addictions*, 1967, 2:53-84.
2. CHERUBIN, C., McCUSKER, J., BADEN, M., *et. al.*: The Epidemiology of Death in Narcotics Addicts. *Am. J. of Epidem.*, 1972, 96:11-22.
3. BRECHER, E. M.: *Licit and Illicit Drugs*. Boston: Littel, Brown and Company, 1972, 101-114.
4. LIGHT, A. B., TORRANCE, E. B.: Opium Addiction—Part VIII. *Arch. Intern. Med.*, 1929, 44:376-394.
5. DOLE, V. P., NYSWANDER, M., KREEK, M. J.: Narcotic Blockade. *Arch. Intern. Med.*, 1966, 118: 304-309.
6. WERNER, A.: Near Fatal Hyperacute Reaction to Intravenously Administered Heroin. *JAMA*, 1969, 207: 2277-2278.
7. WILSON, E. F., FISHER, R. S.: Deaths from Narcotics Use in Baltimore City 1963-1968. *Maryland State Medical Journal*, 1969, 18:49-65.
8. JOHNSTON, E. N., GOLDBAUM, L. R., WHELTON, R. J.: Sudden Death in Heroin Addicts. *Med. Ann. D.C.* 1969, 38:375-380.
9. GOLDBAUM, L. R., WILLIAMS, M., WHELTON, R. J., *et. al.*: The Toxicological Investigation of Sudden Death of Heroin Addicts. Sixth International Meeting of Forensic Sciences (Abstracts), Edinburgh, September 1972.
10. SPECTOR, S., VESELL, E. S.: Disposition of Morphine in Man. *Science*, 1971, 174:421-422.
11. DUPONT, R. L., GREENE, M. H.: The Dynamics of a Heroin Addiction Epidemic. *Science*, 1973, 181:716-722.
12. GREENE, M. H., DUPONT, R. L.: Amphetamines in the District of Columbia. I: The Identification and Resolution of an Amphetamine Abuse Epidemic. *JAMA*, in press, 1973.
13. JAFFE, J.: In *Pharmacologic Basis of Therapeutics* 4th ed., Goodman and Gillman, ed., 1970, 237-275.
14. REYNOLDS, A. K., RANDALL, L. O.: *Morphine and Allied Drugs*. Toronto: University of Toronto Press, 1957, p 119.
15. DREISBACH, R. H.: *Handbook of Poisoning: Diagnosis and Treatment*. Los Altos, Calif., Lange Medical Publications, 1971, p 247.
16. KOLB, L., DU MEX, A. G.: Experimental Addiction of Animals to Opiates. *U.S. Public Health Reports*, 1931, 46:698-726.
17. ALEXANDER, M.: Personal Communication, March 1972.
18. ZAKS, A., FINK, M., FREEDMAN, A. M.: Duration of Methadone Induced Cross Tolerance to Heroin. *Proceedings of the Third National Methadone Conference*, 1970, 54-56.
19. SPECTOR, S.: Personal Communication, February 1972.

* Greene MH, Luke JL, DuPont RL: Opiate Overdose Deaths in the District of Columbia. II—Methadone Related Fatalities. *Journal of Forensic Sciences*, in press July 1974.

** There have been only four heroin overdose deaths reported during the first ten months of 1973.

† Unpublished data, Washington Regional Laboratory, Bureau of Narcotics and Dangerous Drugs.

‡ Garriott JC, Sturner WQ: Morphine Concentrations and Survival Periods in Acute Heroin Fatalities. *N Engl J Med* 289:1276-1278, 1973.

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THE VIEW BOX

Prepared by The Department of Radiology Washington Hospital Center

A white woman in her early twenties was admitted with episodes of renal hematuria. There was no history of hypertension or cardiac abnormalities and no history of renal trauma or coagulation defects.

Excretory Urograms revealed a nonfunctioning kidney on the right. This was followed by a retrograde study which showed filling defects in the renal pelvis suggesting tumor or blood clot. Renal Angiogram was then performed.

(for diagnosis see page 196)



Interactional Behavior in An Alcoholic Community

STEVEN J. WOLIN, M.D. AND PETER STEINGLASS, M.D.

The good life can only be lived in a society in which tidiness is preached and practiced, but not too fanatically, and where efficiency is always haloed, as it were, by a tolerated margin of mess.*

Introduction

Deviant groups have long existed around the boundaries of our communities. Homosexuals, drug addicts, and alcoholic individuals are some of those who, by their recurring encounters with the community at large, repeatedly test the fringes of our morality and conformity. The repeated censuring of offenders and the differential patrolling of specified geographical areas sharpen the boundaries and the norms by which the deviant group will be classified and made known.

Consequently, as Erikson² notes "...deviant behavior is not a simple kind of leakage which occurs when the machinery of society is in poor working order, but may be, in controlled quantities, an important condition for preserving the stability of social life." Erikson goes on to question the benefit derived from deviant behavior by the society. "Can we assume, in other words, that forces operate in the social structure to recruit offenders and to commit them to long periods of service in the deviant ranks? ... deviant forms of conduct often seem to derive nourishment from the very agencies devised to inhibit them."

A community of alcohol addicts, sequestered into a corner of the larger community, illustrates these social phenomena and brings into serious question the "function" of skid row and the likelihood of its eradication by the treatment of individual skid

row members. Skid row has traditionally been the residence for those alcoholic and derelict individuals with a "terminal" (end-stage) social illness. Without home, family, or job the skid row resident is provided with survival but no rehabilitation. Bogue¹ notes that "... the workings of social processes in our contemporary civilization create certain types of circumstances for which society at large accepts

...the purpose is to demonstrate some aspects of the deviant social community which function to preserve its continuity and its distinct relationship with the greater conforming society.

minimal responsibility ... Rather than create a coherent program of help and rehabilitation society temporizes by guaranteeing the men a particular section where they may be watched over and kept under control by police ... Skid row is a combination poor farm and asylum with freedom of movement where the 'patients' are all

regarded as incurable and hence are fed, clothed and housed ..."

It is the purpose of this paper to demonstrate some aspects of this deviant social community which function to preserve its continuity and its distinct relationship with the greater conforming society. We have previously presented a model of alcoholism⁵, based on general systems theory, which demonstrated the stabilizing effect alcohol consumption had on certain kinds of interactional behavior. While the observations which led to this hypothesis of a "drinking system" were made for alcoholism within the intact family^{6,7}, larger social groups might be imputed to regulate and maintain behavior by similar mechanisms.

The drinking system is defined as a system in which behavior is primarily geared toward maintaining conditions which will protect and further the continued consumption of alcohol. At the level of skid row the demonstration of this system would hopefully elucidate important causes for the persistence of this "margin of mess." The following description of one skid row will show how drinking systems stabilize deviant groups and rigidly promote an equilibrium with the rest of society.

The Physical Setting: The Superstructure for the Alcoholic System

Alexandria, Virginia is a small urban

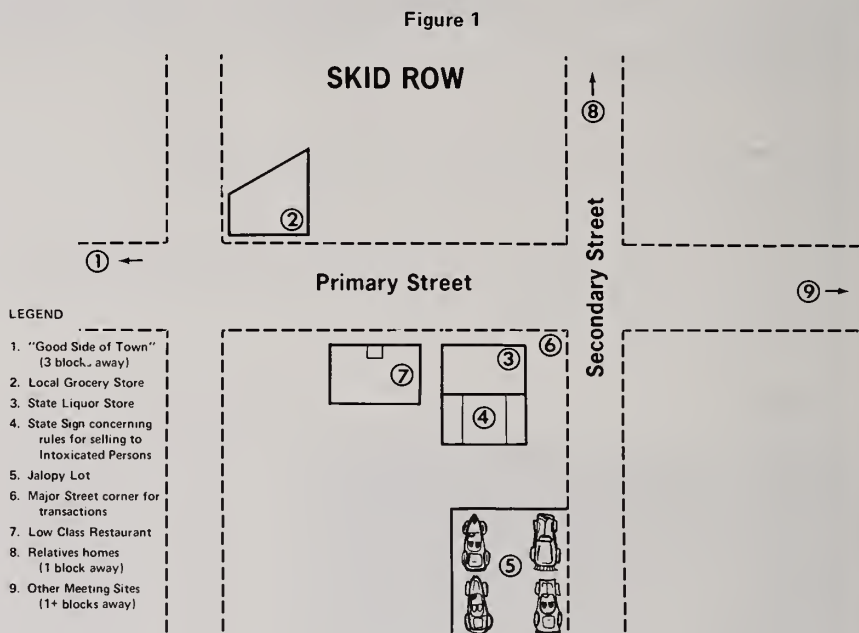
INTERACTIONAL BEHAVIOR IN AN ALCOHOLIC COMMUNITY

WOLIN AND STEINGLASS

community directly adjacent to the Washington, D.C. metropolitan area. Its population of approximately 100,000 is composed largely of middle-class employees of the Federal Government. It is, however, a city with a long history dating back to the revolutionary period, exemplified by the "old town" section of the city, an area with an air of Southern tradition. In contrast to other suburban Washington communities which are typified by single-unit homes and shopping centers, Alexandria is a self-contained urban area and is the shopping and business center for a significant section of Northern Virginia. It has long been struggling with urban problems, one of which is a skid row district and its concomitant alcoholic population. It is estimated that there are 400 alcoholic persons living in a 10-square block region of the City which is identified by City officials and the public as the "skid row".

The authors were introduced to the skid row society by several alcoholic members of the group whom we had met at the local treatment center for alcoholic individuals. They invited us to spend several days with them in this skid row setting to observe their life styles and community. We were introduced primarily as friends rather than as representatives of any organization or institution, and were therefore more easily accepted by the community as observers rather than as intruders.

Diagram #1 is a representative drawing of the skid row setting. It consists of a six square-block area with one primary, two-way, heavily trafficked street and a series of secondary streets which border and intersect it. The primary street contains stores, restaurants and rooming houses which anticipate all the physical needs of the alcoholic persons. About three or four blocks to the East, this same street becomes the "fanciest" one in town. This area, where the towns' people and



most tourists shop, is well patrolled by the police, who assure not only the security of the establishment shopping district, but also enforce a boundary policy vis-a-vis the skid-row community.

It is common knowledge amongst the alcoholic population that everyone must remain "in their place". However, violations of the rule do occur. When a newcomer happens into town one evening he might stray, unknowingly, into the better area of town and attempt to panhandle a middle class woman and her husband. The result of such a mishap (according to the alcoholic community), would be a visit from the local police, who would round up all readily available alcoholic people for a 10-day stay in the local jail. Such episodes, are taken as evidence of the need for the alcoholic community to maintain its inviolate boundaries vis-a-vis the rest of the Alexandria society; each segment of the community must remain out of each other's way.

At the boundaries and across the intersections of this primary street there exist a number of homes, lots and other meeting places which constitute the primary living area for the alcoholic community. Major focal points along the primary street include the small grocery store (no. 2), the local state liquor store (no. 3), the low-class, low-cost restaurant frequented by the transient and indigent population (no. 7), a variety of second-hand clothing stores, and an assortment of hotels. Other, less central, meeting sites include houses along the secondary streets on the diagram (usually homes of relatives), the jalopy lot (no. 5) and more diverse areas such as the cemetery crypts and railroad station approximately a quarter of a mile away. Locales also important to the alcoholic person are the local jail, the Black section of town three blocks away, the prostitutes and drug addicts who live and trade nearby, and the local alcoholism treatment center which is within this district, but off our diagram.

Alcohol as an Organizer of Behavior: A Typical Day on Skid Row

For the alcoholic resident of Alexandria's skid row, the typical day begins between 6 and 7 a.m., when he wakes up to find yesterday's alcohol supply exhausted and his body experiencing the onset of withdrawal symptoms. Despite the repetitious occurrence of this experience, he has once again failed to keep a reserve supply of alcohol to ward off the increasing tremulousness, anxiety and weakness which is rapidly besetting him. All thoughts, therefore, turn to the earliest possible acquisition of the deterrent supply of alcohol.

Since he is often penniless, the addict will awaken from the jalopy lot or the cemetery or his boarding house room or the bedroom in a family apartment and will head for the primary street for some early morning panhandling.

At 7 a.m., the manager of the local grocery store will arrive to open his shop and will invariably be greeted by a group of men standing on the corner in front of his store, to buy the 7% wine that the grocery store can legally sell. Although the store will not officially open until 8 a.m., the manager will sell the men some wine earlier than that for some extra consideration or because he also is an alcoholic and understands their plight. With their initial thirst now quenched, our men will spread out along the primary street to do more serious panhandling. Some of the men might go down to the waterfront or the local labor-pool office where they can receive part-time employment.

By 10 a.m., small groups of three to five men have begun to congregate on the corner near the state liquor store. These groups, which will form and then break up numerous times during the course of the day, provide a major source of social interaction for mem-

bers of the skid-row community. Although the composition of such a group is constantly changing, the format governing its formation, its operation, and its dissolution appears to be remarkably reproducible:

After an initial period of conversation, during which time each member of the group identifies himself and justifies his inclusion in the group, money is pooled for the purchase of a bottle of liquor or wine. Each member's contribution to the pool depends upon his financial resources at the time and seems to bear no relation to the amount of alcohol he will drink from the group bottle after it has been purchased. Following the collection of money, one man is entrusted with the position of "runner". He will now make his way into the state liquor store and purchase the bottle. When the purchase has been made, the runner returns to the group with the bottle of liquor or wine wrapped in a brown paper bag, which he has stuck into his overcoat pocket. The bottle is turned over to the group which then proceeds with the ritual of consuming the alcohol. Consumption may take place at the same street corner where they have been congregating, or they may retire to a place like the jalopy lot. Shortly after the alcohol has been drunk, the group splits up with each individual going off to obtain more money via panhandling, or to his family.

Although individual alcoholic persons will also purchase individual supplies which they can consume by themselves either in their rooms or on the streets, the "bottle gang" remains the major source of social interaction for these men, as described by Rubington.³

As the day progresses, this cycle of building up resources, forming the bottle gang, purchasing and consuming alcohol and breaking up to earn more money occurs repeatedly. Although

disruptions occur which break up the routine, such as an intrusion by a representative of the non-alcoholic society (the police), or a need to satisfy a basic necessity of life such as shopping, food, etc., the basic repetitious pattern remains remarkably the same. Levels of intoxication may fluctuate from day to day and individual drinking patterns may vary within the group, but the basic interactional behavior seems unchanged. Because this interactional behavior is geared so much towards the acquisition and consumption of alcohol, a remarkable degree of stability is created within the skid row community. The cast of characters change, the individual lives are chaotic; yet, the basic form and structure of the interactional behavior, on the level of the bottle gang, looks remarkably stable from day to day.

The State Liquor Store, as the local representative of the government, and, consequently, of the society as a whole, plays a crucial and interesting role in this story. As is true of many governmental agencies, its cold, impersonal glass window is unadorned except for its seal and registry number. Its employees resemble state troopers, wearing a uniform, badge and often sunglasses. Racks of bottles line the rear half of the store and are separated from the patrons by a solid, long counter which also prevents the staff from mingling with customers or from observing any events outside their shop window. This fact is crucial, since a sign, no. 4 on the diagram, over the head of the salesman indicates that the local law is quite explicit; no one who appears intoxicated shall be sold alcoholic beverages.

This physical setting sets the tone for the rest of skid row. To purchase alcohol, not only must the addict panhandle, but he must also corral someone to buy the bottle for him. Fortunately, he can remain on this corner all day, since no one inside the

INTERACTIONAL BEHAVIOR IN AN ALCOHOLIC COMMUNITY

WOLIN AND STEINGLASS

store can see him and he is usually ignored by the police. Similarly, the store itself, knowing its clientele, makes little pretense of its intention to supply alcohol to the local addicted population. It carries cheap wines and whiskeys almost exclusively and remains uncommercial and uninviting. So the day proceeds with behavior almost entirely geared toward the acquisition and consumption of alcohol. The daily routine is simple, routinized and rigid. Available options for behavior seem minimal. Human life has been reduced to a remarkably low level of complexity. For the individual living in this society, decisions are easy because the course of action is to such a great extent predetermined by the requirements attendant to purchasing alcohol and the rules for how one must consume it.

Alcohol as an Organizer of Object Relations

Off the central corner, in the alleyways, unkept lots and deserted parking areas of the skid row neighborhood, most of our subjects congregate for the business at hand, group consumption of alcohol. The men, sitting together in a jalopy which looks almost as disabled as they do, are excessively polite, even formal with each other. Most have some significant physical illness related to chronic alcoholism, such as gastritis, peripheral neuropathy, hepatic failure or an organic brain syndrome, or suffer the indirect effects of their chronic inebriation, such as the pains and cuts resulting from being nightly assaulted on the street. Nevertheless, while sharing their alcohol, they talk little to each other and complain less. One man's withdrawal tremulousness, because he was unable to keep the alcohol down, becomes indistinguishable from a second man's frostbite, a third's ataxia and a fourth's shaking depression. No one appears scape-

goated and the bottle is offered freely and equally to all. They look as if they have been doing this for years together, with little group upheaval and little differentiation from man to man.

The group we studied appeared united in their complaints against the rest of society. They charged the police with harassment and lack of understanding for their problems; they blamed the black population for "ruining" their once safe and clean neighborhood; they saw the alcohol rehabilitation center as alien territory, not as a liaison for treatment. Thus, most of all, they understood their common fate as occupying the lowest rung on the social ladder.

What is the fulcrum for such a group? Is there a pivotal person, a particular relationship or a structural component that allows the group to function as smoothly as it appears to? What is the essential ingredient that defines behavior within this group? What allows these men to live in such apparent intimacy, despite their widely discrepant sociocultural backgrounds? What facilitates the apparent stability of interpersonal relationships within the group despite the wildly chaotic individual psychosocial histories of group members?

The answer to all these questions appears to be *alcohol*. Alcohol serves as the anesthetic and filmy substance that successfully obliterates the differences between one man and another; and allows these men, so different as individuals, to function as a stable organization. Men who apparently would not consider co-existing with each other within the framework of a traditional relationship, accept each other easily when the framework is that of the acquisition and consumption of alcohol.

Comment

We have tried in this paper to

describe how a social system can become organized around alcohol. The systems approach emphasizes that this particular skid row community is a rigidly controlled behavioral organization in which at least two major aspects of human behavior, interaction and object relations, become strikingly simplified because they are carried out almost exclusively within the alcohol framework.

It is easy to see that anyone can plug into this system as long as he follows the simple and clearly defined rules and is willing to relate through alcohol. Some men apparently use the skid-row community as a full-time environment, others float in and out for a two-week binge or on weekends only. But two men might have been drinking together for 10 years in this setting, yet respond, when questioned, that they know nothing more about the other man than his name and how he is handling his current drinking spree.

The systems approach also highlights the fact that this pocket of deviancy within the larger community is maintained not only by its inhabitants, but also by the entire society, as represented by the State Liquor Store and the police. The labelling of these acts as deviant depends upon the perspective through which it is viewed and the feedback of other performers involved in the interactional system.

Perhaps we will have to understand more fully our need to subsidize such deviant behavior before we can successfully institute programs to eliminate it. We must agree with Erikson² who concludes that although the well-structured society appears designed to prevent deviant behavior from occurring, in fact that non-conformity contributes to the survival of the culture as a whole. The deviant and the conformist share a similar set of cultural symbols and mirror one another in their behavior concerning

society's rules. It is likely that the drinking system maintaining skid row will be controlled only when the rest of society resolves its conflict concerning intoxication.

References

1. BOGUE, D.: Skid Row in American Cities. Community and Family Study Center, University of Chicago, 1963, 405-406.
2. ERIKSON, KAI T.: Wayward Puritans: A Study in the Sociology of Deviance. J. Wiley & Sons, Inc., New Jersey, 1966, 8-23.
3. RUBINGTON, E.: The Bottle Gang. Quart. J. Stud. Alc. 29:943-955, 1968.
4. RUBINGTON, E.: The Changing Skid-Row Scene. Quart. J. Stud. Alc. 32:123-135, 1971.
5. STEINGLASS, P., WEINER, S. MENDELSON, J.: A Systems Approach to Alcoholism: A Model and its Clinical Application. Arch. Gen. Psychiat. 24:401-408, 1971.
6. STEINGLASS, P., WEINER, S. MENDELSON, J.: Interactional Issues as Determinants of Alcoholism. Amer. J. Psychiat. 128:275-280, 1971.
7. WEINER, S., TAMERIN, J., STEINGLASS, P., et al: Familial Patterns in Chronic Alcoholism: A Study of a Father and Son during Experimental Intoxication. Amer. J. Psychiat. 127:1646-1651, 1971.

* Aldous Huxley, Prisons: The Carceri Etchings by Pirenesi, The Trianon Press, London, 1949, p. 13.

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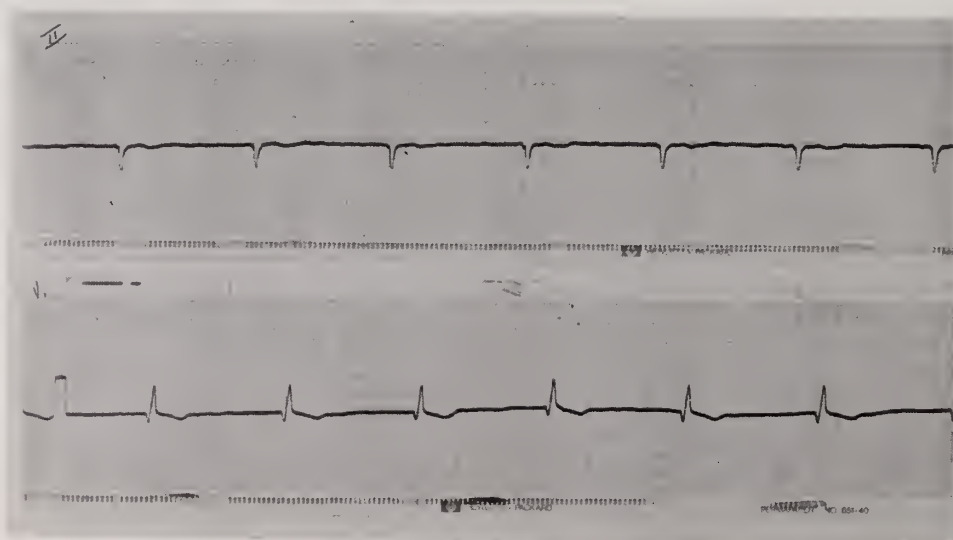
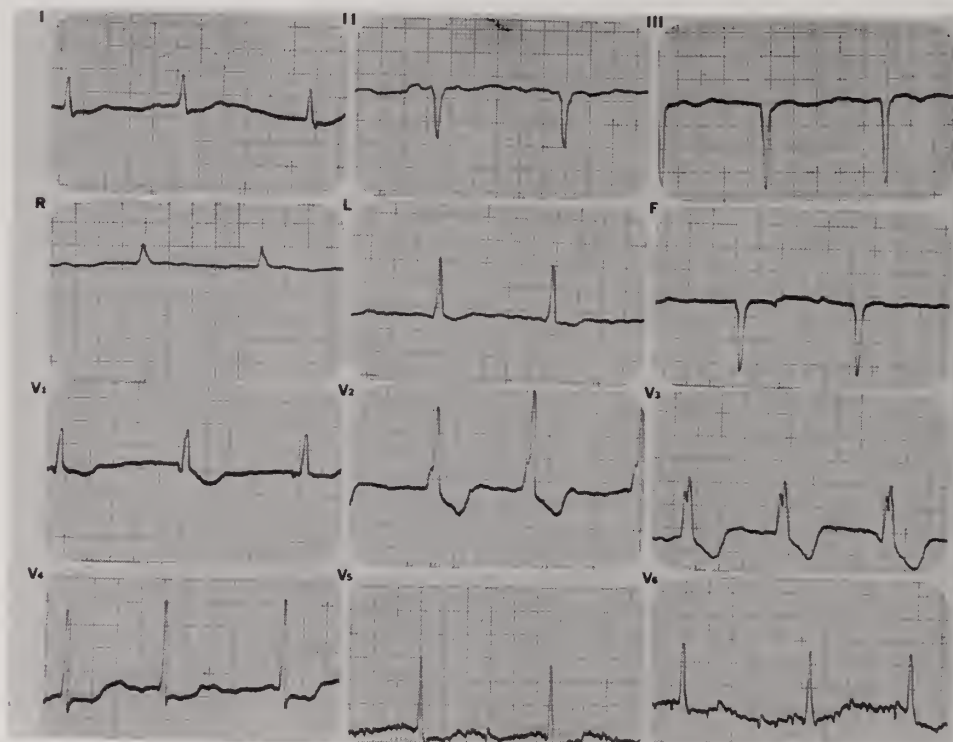
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ECG PROBLEMS

HISTORY: A 91-year-old white woman with a long history of coronary heart disease and congestive failure controlled well with Digitalis. Tracing No. 1. is a characteristic electrocardiogram similar to those she has had for two or three years. The longer portions of Leads II and V₁ were taken from an electrocardiogram obtained on admission to the hospital because of increased symptoms and signs of congestive heart failure.

(for diagnosis see page 196)



Colonoscopy—Fiberoptic Endoscopic Approach to the Colon and Polypectomy

DAVID C. WHERRY, M.D. AND HARRY ZEHNER, JR., M.D.

Abstract

The introduction of the fiberoptic colonoscope has given us a new method of removal of polypoid lesions of the colon as well as a new method to study colonic disease. Polypectomy can be performed with a low morbidity and mortality, providing that the operative surgeons develop some expertise before using the colonoscope. The obvious advantages to the patient, as well as reduction of time lost from work and expense incurred while in the hospital, are additional reasons for using this method of polypectomy.

Introduction

There has never been any controversy about the management of polyps visible through the rigid sigmoidoscope—they are all quickly resected and examined microscopically. No labored rhetoric, no wringing of hands accompanies this decision. Until recently polyps above the sigmoid were the object of great concern and disagreement as to management. The technique of "polyp watching" resulted in increased exposure to radiation, delays in early operation on potentially curable carcinomas and considerable psychological strain to patients. Exploratory laparotomy on the other hand exposed the patient to the risks of operative mortality and morbidity. The operation was further complicated by the limitations of frozen section diagnosis, technical prob-

...fiberoptic colonoscopy which enables an operator to visualize the entire lumen of the colon from ileocecal valve to anus and to remove polyps and specimens at will.

lems of multiple colotomies, and the possibility that additional small polyps were missed even at laparotomy. All this has changed with the introduction of fiberoptic colonoscopy which enables an operator to visualize the entire lumen of the colon from ileocecal valve to anus and to remove polyps and specimens at will. Polyp management is now simple, rational and safe.

With the stimulation and help of Dr. Steven Hedberg of the Massachusetts General Hospital we began colonoscopy in February 1973, with the use of the ACMI fiberoptic colonoscope.

Technique of Polypectomy Through the Colonoscope

Colonoscopic examination is indicated for patients of almost any age who exhibit gross or occult rectal bleeding, obscure x-ray findings, polyps visible on x-ray examination or the presence of inflammatory bowel disease.

It is also useful in post-operative examination of the colon. In general, patients should not undergo colonoscopy if they are suffering from perforating disease of the colon, peritonitis, acute conditions of the anus and rectum, recent abdominal surgery or recent myocardial infarction. Examination may be difficult, though not necessarily contraindicated, in patients who have had previous pelvic surgery or previous pelvic inflammatory disease. Examination is also rather difficult in patients with markedly redundant bowel.

Patients are prepared by placing them on a light diet or liquid diet for 3 days prior to the examination, with two ounces of castor oil the evening before the examination and a cleansing enema that evening and approximately an hour before the colonoscopy the following day. The procedures have all been performed in the operating room. The majority of patients are admitted the morning of the operative procedure with their history and physical examination recorded and routine laboratory work done the day prior to the surgery.

The patients were informed that if a complication developed during or after the operative procedure it might well be necessary for an abdominal laparotomy to be performed and the problem corrected (the two major complications reported in the literature have been bleeding from the pedicle or biopsy site, and perforation). An operative permit for laparotomy is signed prior to the surgery.

FIBEROPTIC COLONOSCOPY

WHERRY AND ZEHNER

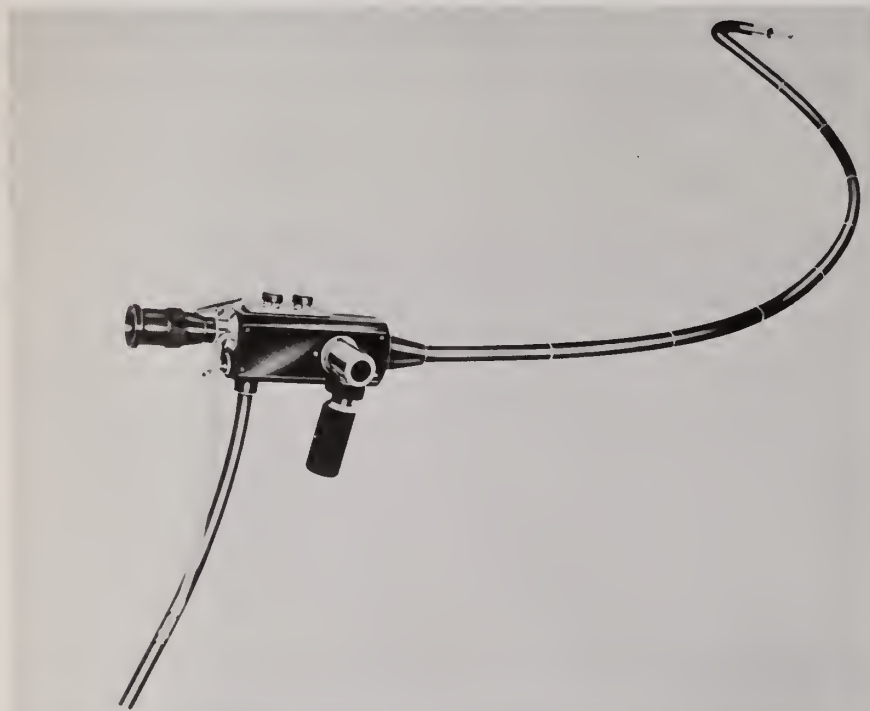


Figure 1: ACMI 160 cm. Colonoscope with a F7 and F12 Channels.

All of these procedures were done under analgesia or light anesthesia using combinations of Talwin, Demerol, Valium and Pentothal. The procedure begins with the patient in the left lateral or Simm's position. The rectum is dilated. If the preparation of the patient appears inadequate a routine proctoscopy is done and the fluid contents are suctioned off prior to introduction of the colonoscope. It is preferable to have a teaching attachment to the colonoscope so that the operator as well as the assistant can see the introduction and passage of the colonoscope. The assistant pushes the instrument as the operator works the control and visualizes the lumen.

The instrument is first passed to its entire length, or to the entire depth that one is able to pass it, before any operative procedures are performed. The technique of passage of the

instrument has been well described by Rogers.³ The most difficult part of the colon to pass usually is the sigmoid colon. It may be quite redundant or looped. In addition, numerous diverticula may be present which make passage difficult. It is interesting to study the anatomy and the pathology of these diverticula. The passage of the instrument up the descending colon is usually uneventful, with the next difficulty encountered at the splenic flexure where one must turn the corner into the transverse colon. The redundancy of the transverse colon will determine the problems at this corner. The transverse colon is recognized by the triangular appearance of the haustral folds. The instrument is then passed on towards the hepatic flexure.

In passing the colonoscope, the tip must be the part that moves. If one

has a looped or redundant sigmoid colon one begins to stretch the colon without advancement of the tip of the instrument, so that a considerable length of the colonoscope may be introduced; thus, without any advancement of the tip one is looping the instrument.

After the instrument has been passed to its full length the position of the end of the instrument can sometimes be determined by seeing the light of the scope through the abdominal wall of the patient. If one is confident by this method that the level is known, the scope can be withdrawn and polyps detected and removed. If not, it is best to take one portable x-ray with the scope completely introduced to determine the total extent of colonic instrumentation.

As the colonoscope is withdrawn the most distal polyp identified is usually removed first. This is done by passing a wire snare with a plastic cover down the instrument, opening the loop, passing it around the polyp and (if it is pedunculated) removing the polyp about mid way down the stalk. The snare is a soft snare and will not in itself cut across the polyp; therefore, one burns across the stalk using electric current. This insures that the stalk is adequately cauterized and that no bleeding will occur. If the polyp is caught on the snare the instrument and snare can be removed together with the polyp and sometimes visualization of the remainder of the colon can be performed with the polyp being carried out with the instrument. In the majority of cases, however, it will be necessary to locate the polyp after it has been removed from the wall of the bowel and to suck in into the end of the instrument. Then the polyp and entire instrument must be withdrawn and the instrument re-introduced to continue the examination of the colon, as well as to perform additional polypectomies.

Small polyps the size of a 12 french catheter can be withdrawn through the large channel of the operative scope.

If the polyp is lost and cannot be retrieved, the patient is given a cleansing saline enema after the operative procedure and the polyp recovered. If the polyp remains too long in the bowel without recovery it will be autolysed and pathological examination will be impossible.

There are now new models of polypectomy graspers with tenaculums which can be introduced through the instrument. These will allow one to grasp the polyp and recover it without having to suck it into the instrument.

Prior to cauterization of the polyp it is advisable to flush the colon out with CO₂ to avoid any chance of explosion from the hydrogen and methane which are ordinarily present in the colon.

If one finds difficulty in passage of the instrument the patient is usually turned into the lithotomy or right lateral position. This often facilitates passage. Occasionally gentle abdominal palpation may help pass the tip of the instrument.

Discussion

In the past year we have done 43 polypectomies on 40 patients. There has been no mortality or morbidity. The majority of these patients presented with asymptomatic polyps of the colon from the hepatic flexure to the mid sigmoid colon which had been picked up on routine barium enema done during annual physical examinations. The polyps ranged in size from 1.5 to 3.0 cm. in size. They were both sessile and pedunculated and there was no evidence of carcinoma in any of the polyps removed.

Wolff and Shinya¹ reported a total of 2,000 colonoscopies done in their endoscopic unit where 499 polyps were removed from 350 patients. Of this group, 9.4% of the polyps were of

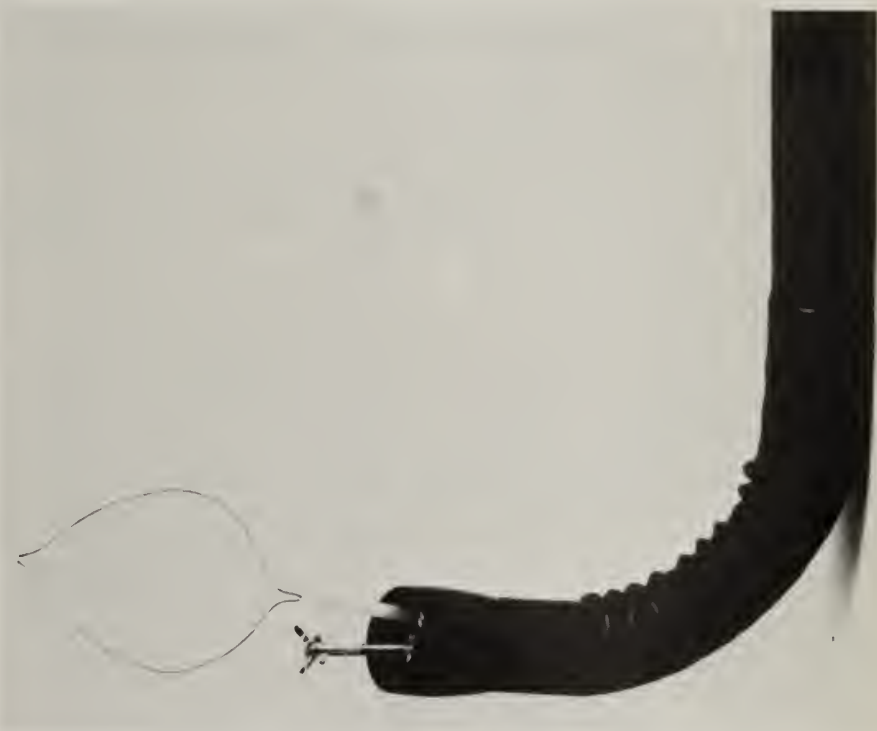


Figure 2: Soft Wire Biopsy Loop.

the sessile type, the remainder were pedunculated. Of the polyps excised, 6.8% revealed evidence of malignant change with 3.4% of the polyps showing invasion at least through the *muscularis mucosa*.

In the series of 17 malignant polyps removed by Wolff and Shinya,¹ 13 patients underwent operation. In the others it was deemed that endoscopic resection accomplished complete removal. Of the 13 patients, in one the surgeon could find no evidence of a residual lesion. In the other 12 colons which were resected 7 showed no residual tumor and in 5 residual tumor was present. In one of these patients a lymph node metastasis was present.⁵ The patient had, in addition to a malignant polyp, an endoscopically recognized and biopsied adjacent small ulcerating adenocarcinoma. Wolff¹

cautions against losing sight of an early cancer while one is focusing his attention on removal of a polyp. Satellite polyps have been reported in association with 25 to 50% of colon carcinomas.^{11,12,13,14} Patients with multiple polyps are twice as likely to develop a colon cancer as the patient with a single polyp.

Morson^{8,9,10} states that in patients who have had a colon resected for cancer, if polyps are present in the specimen the chance of developing another cancer of the colon is doubled.

In April, 1973 at the Annual Meeting of the American Surgical Association Dunphy¹ stated that fiberoptic colonoscopy and polypectomy will essentially eliminate the need for abdominal laparotomy in the control of colonic polyps. Recent articles includ-

FIBEROPTIC COLONOSCOPY

WHERRY AND ZEHNER

ing those of Marks *et al.*,² Williams,⁵ Richter⁶ and Yuxhvidova⁷ all tend to indicate that most polyps of the colon can be removed via the colonoscope once one acquires the necessary expertise, and that it can be accomplished with a high degree of safety.

As with all operative procedures, complications have developed and the procedure has its limitations. As mentioned before, in patients with a rather wide sigmoid loop it will be difficult to pass the tip of the instrument to any great depth. Patients that have adhesions which preclude getting around the difficult bends of the colon are not good candidates for this procedure.

Welch¹ states that in the next year or two the whole history of polyps and of early cancer of the colon will undergo important revisions because of the data obtained by this method. The importance of this statement is already being revealed by Wolff and Shinya¹ in that they are noticing both adenomatous and villous mucosal features in the same polyp.

Sugarbaker¹, quoted by Moore, by April, 1973 had done 355 colonoscopies with removal of 109 polyps ranging in size from 0.5 to 3.0 cm. 10% of their polyps were malignant, one-half of these were invasive. They had three complications: one bleed requiring operation and two free perforations. Since these patients have a colon relatively well prepared prior to surgery, perforations of the colon sometimes display minimal clinical symptoms. The physician must have a high index of suspicion and check by x-ray for free air if there is a sharp pain at the time of cauterization of the polyp. Also noted are 14 patients in whom the radiologist could not make a distinction between diverticulitis and carcinoma, and that the colonoscopy had made the diagnosis correctly in all of the cases. In all the patients with polyps who had had preoperative measurement of their carcinogenic em-

bryonic antigen, none had positive assays even though the polyp was malignant.

Schrock,¹ quoted by Dunphy, has done three hundred colonoscopies and seventy polypectomies without complication except for one moderate hemorrhage.

Personal communication with Hedberg¹⁵ reveals that he has done 247 polypectomies with the complications of four perforations and two hemorrhages. One of the hemorrhages required surgery for a ruptured spleen and the other was bleeding from a pedicle which required transfusion. The four perforations occurred in patients with sessile polyps of the colon and in one villous adenoma with carcinomatous changes. He stresses the importance of the difficulties in removing sessile polypoid lesions and the possibility of perforation. They have removed 173 adenomatous polyps without complication and have had no complications with polyps less than 2.0 cm. in diameter. The difficulties have been with large and sessile polyps.

References

1. WOLFF, WILLIAM I., M. D., SHINYA, HIROMI, M. D.: A New Approach to Colonic Polyps. *Annals of Surgery*, September 1973, Vol. 178, No. 3, pp. 367-378.
2. MARKS, GERALD, M. D., MOSES, MELVIN LLOYD, M. D.: The Clinical Application of Flexible Fiberoptic Colonoscopy, *The Surgical Clinics of North America*, June 1973, pp. 735-756.
3. ROGERS, B. H. GERALD, M. D.: Technique of Coloscopy, December 26, 1972, pp. 1-24.
4. FRIEND, WILLIAM G., M. D.: Technique for Coloscopy and Polypectomy, pp. 1-3.
5. WILLIAMS, C. B.: Colonoscopy: An Air-Pressure Hazard, *The Lancet*, September 29, 1973, p 729.
6. RICHTER, ROBERT M., M. D., FACS: Intraoperative Fiberoptic Colonoscopy, *Arch Surg.*, Vol. 106, February 1973, p 228.

7. YUKHVIDOVA, G. M., D M: Colonoscopy, *The American Journal of Proctology*, October 1973, Vol. 24, No. 5, pp. 392-395.
8. MORSON, B. C.: Control and Prevention of Intestinal Cancer. *Brit. J. Hospital Med.*, 1839, Nov. 1969.
9. MORSON, B. C.: Precancerous and Early Malignant Lesions of the Large Intestine. *Brit. J. Surg.*, 55:48, 1968.
10. MORSON, B. C., BUSSEY, H. J. R.: Predisposing Causes of Intestinal Cancer. *Curr. Probl. Surg. Year Book Medical Publishers, Inc.*, Chicago, 1970.
11. GROSBERG, S. J., GALAMBOS, J.: The Relationship of Polyps to the Survival of Patients Operated on for Carcinoma of the Large Bowel. *Gastroenterology*, 44:33, 1963.
12. HELWIG, E. B.: Adenomas and the Pathogenesis of Cancer of the Colon and Rectum. *Dis. Colon Rectum*, 2:5, 1959.
13. SWINTON, N., WEAKLEY, F.: The Early Diagnosis of Carcinoma of the Colon and Rectum. *Lahey Clinic Found. Bull.*, 12:227, 1962.
14. WELCH, CLAUDE E.: Polypoid Lesions of the Gastrointestinal Tract. W. B. Saunders Co. Philadelphia, 1964.
15. HEDBERG, S.: Personal communication.

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Intraventricular Hematoma Successfully Treated by Surgery

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Abstract

Intraventricular hematomas of spontaneous or traumatic origin, although infrequent, constitute a distinct entity which should be considered. The authors present the case of such a hematoma successfully treated by surgery. A review of the literature is also provided.

Introduction

Intraventricular hematomas are rarely seen in neurosurgical practice and also have rarely been reported in the literature. Even more rare is their association with trauma. The following case of a hematoma of the lateral ventricle, successfully treated by surgery, is presented to bring this clinical entity into focus.

Case Report

A 39-year old man was brought into the emergency room after being found unconscious in the basement of his house. No reliable history was available, although a vague history of a fall preceding his unconsciousness was obtained. Additional information, given subsequently by the patient's sister, reported him as having been in good health and without any significant complaints. The patient was lethargic but easily arousable, responding to commands, and without any gross neurological deficit. Blood alcohol de-

termination demonstrated levels of 220 mg%. He was kept overnight for observation.

The next morning the patient was more obtunded and a neurosurgical consultation was requested. Examination described the patient as lethargic, responding to simple commands, and complaining of headache. There was moderate nuchal rigidity and slight weakness of the left extremities. The deep tendon reflexes were slightly increased on the left. No pathological reflexes were present. The fundi were

60,000, white cell count: 2,610 with 90% polymorphonuclears. X-rays of the skull showed a linear fracture across the right frontal bone.

A cerebral angiogram was performed by right retrograde brachial injection. This showed evidence of marked ventricular dilatation, without any shift of arterial or venous structures or other abnormality. A brain scan was also performed which was normal.

In the course of the day the patient's neurologic status remained unchanged; however, during the evening of the same day his condition started to deteriorate. He lapsed into deep stupor with pinpoint pupils and occasional Cheyne-Stokes respiration, and his temperature rose to 103° F.

An air-ventriculogram was performed. About 10 cc of old hematoma were obtained followed by clear, slightly xanthochromic cerebrospinal fluid—CSF. X-rays were taken which showed marked dilatation of the lateral ventricles without evidence of ventricular shift. Because of the patient's condition, a Scott ventricular cannula was inserted in the right lateral ventricle and connected to external ventricular drainage. Immediately following this procedure, the patient's level of consciousness improved and so remained during the course of the night.

The next morning the CSF in the ventriculostomy catheter was clear, but the patient was again stuporous. At this time a conjugate deviation of

...after review of the literature, this appears to be the first traumatic intraventricular hematoma successfully treated by surgery.

normal. His temperature was 102° F, his blood pressure was 140/80, pulse 80/min., and respirations 24/min. The remainder of the physical and neurological examination was within normal limits except for a very marked thoracolumbar scoliosis. There was no external evidence of head (or other) injury. Lumbar puncture was done and yielded grossly bloody fluid with a xanthochromic supernatant. The protein was 1.6 gr.%, the red cell count:

INTRAVENTRICULAR HEMATOMA TREATED BY SURGERY

KOULOURIS, FATEHI AND COONEY

his eyes to the left was added to his overall picture. A Conray ventriculogram was performed, which confirmed the previous air-ventriculogram findings and, in addition, demonstrated a large right frontal intraventricular mass.

A right frontal craniotomy was performed. The brain appeared normal, without evidence of recent trauma or hemorrhage. The right frontal ventricular horn was entered and a large semi-solid hematoma was encountered. This was removed with a combination of gentle suction and blunt dissection. In the course of the removal, the hematoma was seen to extend to and through the foramen of Monro to the opposite ventricle. This part of the hematoma was also easily removed by suction. After complete evacuation, the entire ventricular cavity was inspected and no evidence of vascular anomaly or other pathologic change was seen over the walls or the floor of the ventricle. No biopsy of the ventricular wall was attempted for fear of initiating new hemorrhage. Various sections of the surgical specimen showed organized hematoma without any evidence of vascular or other abnormality. The patient tolerated the procedure well and had an uneventful postoperative course which was complicated by a short period of inappropriate antidiuretic hormonal secretion. The patient also developed a communicating hydrocephalus, requiring a right ventriculoatrial shunt. At this time (five months after surgery) the patient has made progressive recovery. He is alert with good motion in all extremities. His shunt is still functioning and he is receiving intensive physical therapy.

Discussion

An extensive literature has been devoted to the subject of intracerebral hemorrhage and hematoma, dealing in detail with its etiologic, diagnostic,

and therapeutic aspects. Very little attention has been given, however, to intraventricular hemorrhage and hematoma as such, and very seldom has it been envisaged as a distinct entity. The first cumulative report is that of Sanders¹¹ who, in 1881, undertook an analysis of 94 cases of intraventricular hemorrhage found at autopsy; his report constitutes a true classic in the neurological literature. During the first part of the 20th century, intraventricular hemorrhage, although recognized, was generally considered as a complication or extension of intracerebral hemorrhage. The commonly accepted opinion was that intraventricular hemorrhage (IVH) usually caused death within a few hours.

Classically, these hemorrhages occur in individuals with arteriosclerosis and/or hypertension, or in patients with vascular anomalies. IVH is also well recognized as a common cause of death in premature infants, resulting usually from hemorrhage of the terminal vein.⁹ These intracerebral intraventricular hemorrhages are characterized by the acute onset of severe headache and loss of consciousness, and the presence of bloody cerebrospinal fluid. Frequently there are signs of hypothalamic and brainstem involvement, such as hyperthermia, fixed pinpoint pupils, and decerebrate rigidity. If the hemorrhage begins in one hemisphere, there may be contralateral seizures or hemiplegia early in the course, but these signs often disappear as the bleeding continues and the entire ventricular system fills with blood. Death usually occurs within less than 48 hours.

The entire constellation of signs and symptoms of IVH has been well discussed by Gordon⁶ in 1938 and by Steel¹³ in 1941. This subject has also been examined by McNealy and Plum⁸ in a series of autopsy cases, as well as by Crawford and Dorothy Russell.⁴ Little attention has been given, however, to the fact that an intraventricu-

lar hemorrhage may eventually have a less acute course and, at times, progress to the formation of a discrete hematoma which in turn might even simulate an intraventricular tumor. Little mention has been made in the literature of this latter phenomenon. Dandy⁵ reported, in 1933, one case of venous aneurysm of the wall of the lateral ventricle which ruptured into the brain substance and subsequently extended into the temporal horn. The dynamic pathology in this case, however, may be considered as that of a secondary intraventricular extension of an intracerebral hematoma, rather than a primary intraventricular one. The first documented cases of intraventricular hematoma were reported by Avol and Vogel¹ in 1955. Their first case was that of a 48-year old man with a long history of headaches who demonstrated clinical and radiographic evidence of intraventricular tumor. He was operated upon with excellent results. Their second case was that of a 14-year old boy with an 18 month history of headaches; at surgery, an intraventricular hematoma was found along with a miniscule vascular malformation of the choroid plexus. The operative results were also excellent in this case.

Carton and Alvord³ reported, in 1957, four cases of intraventricular hematomas, two of which underwent surgery. One of these was in a 38-year old man with sudden onset of subarachnoid hemorrhage and coma. Angiography and surgery disclosed the presence of intraventricular hematoma along with an arteriovenous malformation of the head of the caudate nucleus. Their second case was that of a 57-year old man with sudden subarachnoid hemorrhage and coma. Both had good recovery after surgery. Their two remaining cases were those of a 72-year old man and a 29-year old man, both hypertensive, with sudden onset of coma. Intraventricular hematomas were found at autopsy. Caram,

Sharkey and Alvord² have reported (1960) a patient with an aneurysm of the anterior choroidal artery, associated with intraventricular hematoma, which was surgically removed. The patient did not survive the operation and at autopsy an arteriovenous malformation of the basal ganglia was also found which, even in retrospect, was not seen in any of the three preoperative angiograms. Murtagh and Baird⁹ in 1961 presented two cases of circumscribed intraventricular hematoma in infants both associated with craniosynostosis. Both patients underwent surgery, one with excellent results and the second with death after six months from secondary arachnoiditis and hydrocephalus. The etiology in these two cases might be postulated as being birth trauma, although a high incidence of intraventricular hematoma has been found during fetal autopsies in which no traumatic factor was involved. Two surgical cases were reported by McDonald⁷ in 1962; in both cases the hematoma involved the third ventricle and neither patient survived surgery. Autopsy was performed in only one case and no other intracerebral pathology was detected. Ojemann and New¹⁰ in 1963 reported the first and only case in the literature of intraventricular hematoma well documented by x-rays and not surgically treated. This hematoma was associated with an arteriovenous malformation involving the posterior cerebral artery and the vein of Galen, and resolved spontaneously over a period of nine months as this was documented by follow-up air-encephalography. The patient had a complete functional recovery. Finally, Schürmann, Brock and Samii¹² reported in 1968 the successful removal of an intraventricular hematoma associated with an aneurysm of the lenticulostriate artery which was also successfully clipped.

The present case adds one more to the series of 13 cases of intraventricular hematoma retrieved from the litera-

ture. Out of the 14 cases, 11 have been operated upon with seven survivals and four deaths. Of the four deaths, two underwent autopsy. Of the three non-surgical cases, two were discovered at autopsy. In five cases a vascular anomaly was also present. In the remaining no etiology could be found, although in two birth trauma was possible. Interestingly enough, 12 out of 14 patients were males.

In the present case, one can only speculate on the role of trauma. Considering the inadequate history and the sequence of events, it is difficult to ascertain whether the intraventricular hemorrhage with the subsequent hematoma preceded and caused the fall or were its after effects. The possibility of this being a traumatic hematoma, secondary to head injury from the fall, seems more likely. On the same basis and after review of the literature, this appears to be the first traumatic intraventricular hematoma successfully treated by surgery.

References

1. AVOL, M., VOGEL, P.: Circumscribed intraventricular hematoma simulating an encapsulated neoplasm. *Bull. Los. Aug. Neurol. Soc.* 20: 1955, 25-29.
2. CARAM, P. C., SHARKEY, P. C., ALVORD, E. C., JR.: Thalamic angioma and aneurysm of the anterior choroidal artery with intraventricular hematoma. *J. Neurosurg.* 17: 1960, 347-352.
3. CARTON, C. A., ALVORD, E. C., JR.: Localized intraventricular hematoma. *J. Neurosurg. exp. Neurol.* 16: 1957, 113-114.
4. CRAWFORD, J. V., RUSSELL, D. S.: Cryptic arteriovenous and venous hematomas of the brain. *J. Neurol. Neurosurg. Psychiat.* 19: 1956, 1-11.
5. DANDY, W. E.: Benign encapsulated tumors in the lateral ventricles of the brain; diagnosis and treatment. *Ann. Surg.* 98: 1933, 841-845.
6. GORDON, A.: Primary ventricular hemorrhage. *Arch. Neurol. Psych.* Chicago 39: 1938, 1272-1276.
7. McDONALD, J. V.: Midline hematomas simulating tumors of the third ventricle. *Neurology* 12: 1962, 805-809.
8. MCNEALY, D. E., PLUM, F.: Brain-stem dysfunction with supratentorial mass lesion. *Arch. Neurol.* 7: 1962, 10-32.
9. MURTAGH, F., BAIRD, R. M.: Circumscribed intraventricular hematoma in the infant associated with craniosynostosis and secondary hydrocephalus. *J. Pediat.* 59: 1961, 351-355.
10. OJEMANN, R. G., NEW, P. F. J.: Spontaneous resolution of an intraventricular hematoma. Report of a case with recovery. *J. Neurosurg.* 20: 1963, 899-902.
11. SANDERS, E.: A study of primary immediate or direct hemorrhage into the ventricles of the brain. *Amer. J. Med. Sci.* 82: 1881, 85-128.
12. SCHURMANN, K., BROCK, M., SAMII, M.: Circumscribed hematoma of the lateral ventricle following rupture of an intraventricular saccular arterial aneurysm. *J. Neurosurg.* 29: 1968, 195-198.
13. STEEL, R. S.: The diagnosis of intraventricular hemorrhage. *Med. J. Aust.* 2: 1941, 647-649.

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THE VIEW BOX

(from page 182)

DIAGNOSIS: CONGENITAL ARTERIOVENOUS FISTULA

Arteriovenous fistulae have been described following total or partial nephrectomy, following renal biopsy and blunt or penetrating trauma. Fistulae can be seen with very vascular renal cell carcinomas and on a congenital basis.

This lesion is associated with, or responsible for, hypertension, congestive failure and flank pain. In 20% it can cause hematuria.

Note in the Angiograms the conglomerate of arteriovenous channels in the lower pole and the early visualization of the main renal vein and inferior vena cava.

Treatment in this case consisted in nephrectomy but increasing numbers of patients are being treated with embolization of either homologous clot or muscle emboli through selectively placed catheters.

*Edited by Gunther J. Augustin, M.D.
Senior Attending Radiologist, Washington
Hospital Center, Washington, D.C.*

ECG DIAGNOSIS

(from page 188)

INTERPRETATION:

Figure 1:

1. Atrial fibrillation.
2. Incomplete right bundle branch block with left anterior hemiblock.
3. ST-T wave abnormalities probably indicating Digitalis effect as well as those changes which are secondary to the conduction abnormality.
4. Probable old inferior myocardial infarction.

Figure 2: The conduction abnormalities are still present and the patient is still in atrial fibrillation. However, there is now complete A-V block with a junctional focus driving the ventricles. This explains the regular ventricular rhythm in the presence of atrial fibrillation. This is a manifestation of digitalis toxicity.

This rhythm can only be diagnosed by the electrocardiogram. Whenever a patient who is in atrial fibrillation develops a regular cardiac rhythm, an electrocardiogram should be taken in order to determine whether he has returned to sinus rhythm or is digitalis toxic and has developed junctional rhythm with A-V block. Digitalis was discontinued in this patient, she improved, and three days later demonstrated the expected irregular ventricular rhythm with atrial fibrillation.

Edited by Robert R. Montgomery, M.D.

Multiple Excavating Pulmonary Metastases

DAVID SIMON, M.D.

Abstract

A 44 year old man was found to have multiple excavating pulmonary metastases from a primary squamous cell carcinoma of the esophagus. Cavitation in tumors metastatic to the lung is not extremely rare. Nearly 100 such cases have been reported. The primary tumors which metastasize to the lung are usually either squamous cell carcinoma (44%) or adenocarcinoma (36%), whereas bronchogenic carcinoma with cavitation is predominantly squamous cell (72–82%). Possible mechanisms of cavitation include 1) obstruction of airways with subsequent infection, 2) loss of blood supply, 3) desquamation and liquefaction within squamous cell tumors, and 4) cell autophagism.

Introduction

Pulmonary cavities are so frequently due to bacterial infections that other causes are often not considered in their differential diagnosis. However, neoplasms excavate frequently enough to need to be included in the differential diagnosis of pulmonary cavities. Cavities may be of two varieties; those due to bronchial obstruction with distal infection, and those due to cavitation of the tumor itself without obstruction. The purpose of this report is to record the occurrence of multiple cavities due to cancer metastatic to the lung.



Case Report

C. C., a 44 year old white male construction worker, was admitted to the Washington Veterans Administration Hospital with progressive dysphagia for one year and a weight loss of 75 pounds. He had been a heavy cigarette smoker and a heavy drinker. For several years he had a chronic cough, which produced sputum only in the mouth prior to admission. He denied fever and night sweats. Physical examination revealed a wasted, dehydrated man in no distress, with a temperature of 96°, a pulse of 80, respirations of 30, and a blood pressure of 95/70. Pertinent findings were a firm, nontender, 3 cm left submandibular mass, a barrel shaped chest, hyperresonance to percussion with scattered wheezes, rhonchi, and fine rales bilaterally. There was a firm, nontender 4 x 7 cm mass over the proximal radial aspect of the right forearm.

The hematocrit was 37%, leukocytes 12,000/mm³, neutrophils 82%, bands 4%, lymphocytes 13%, monocytes 1%; the bilirubin was 0.9 mg %, alkaline phosphatase 11 King Armstrong units, total protein 7.0 gms %, albumin 2.6 gms %. The arterial blood gases were PaO₂ 59 torr, PaCO₂ 33 torr, with a pH of 7.43. Stains and cultures were negative for mycobacteria.

The chest x-rays (left) show extensive bilateral cavitation with infiltrates. An x-ray taken two years

MULTIPLE EXCAVATING PULMONARY METASTASES

SIMON

previously was normal. A gastrographin study of the esophagus revealed a 10 cm area of marked narrowing with complete disruption of the mucosal pattern and dilatation of the proximal esophagus. Contrast material appeared in the bronchial tree, indicating a bronchoesophageal fistula. Esophagoscopy confirmed the presence of a mass which biopsy revealed to be a poorly differentiated squamous cell carcinoma. Bronchoscopy confirmed the presence of a bronchoesophageal fistula. A feeding gastrotomy was performed on the fourteenth hospital day. The patient expired on the twentieth hospital day.

Autopsy findings revealed carcinoma of the esophagus with multiple lung metastases, with cavitation, within all lobes. All cavities were lined with tumor cells. There were metastases to the heart, liver, adrenal glands, kidneys, bone (including the right forearm mass), and multiple lymph nodes.

Discussion

Although this case has unusually extensive cavitation due to malignancy, cavitating pulmonary metastases are not extremely rare. Since LaForet and LaForet¹ reviewed non-tuberculous cavitory disease and included six cases of pulmonary metastases, there have been several series^{2,3,4} and case reports comprising nearly 100 such cases. Cavitation was detected in 4% of metastatic tumors (398 cases) and 9% of primary lung tumors (176 cases) by Dodd and Boyle.² In other series^{7,13} of primary carcinoma of the lung, the prevalence of roentgenographic cavitation has ranged from 2% to 7%. As expected, the prevalence by pathologic examination is higher. Chaudhuri¹⁷ found necrosis and cavitation in 100 cases out of a total of 632 (16%) primary bronchial carcinomas at autopsy.

When evaluated by cell type, the majority of primary lung cancers with cavitation were squamous cell. In a series of reports by Lehar *et al.*⁷ and Byrd *et al.*^{8,9,10} cavitation was found in 22% of cases with squamous cell carcinoma, in 4% of cases with large cell carcinoma, and in 2.4% of cases with adenocarcinoma; no instances of cavitation were found in 114 cases of small cell carcinoma at autopsy. Of the 25 cases showing cavitation, 72% were squamous cell, 16% were large cell, and 12% were adenocarcinoma. Strang¹¹ had similar findings in that squamous cell comprised 82% of 44 cases of cavitating lung carcinoma. Chaudhuri, also, found 82% squamous cell as well as 11% large cell, 4% adenocarcinoma and 3% alveolar-cell carcinoma in his series of 100 cases of primary cavitating carcinoma.¹⁷ There are also at least two case reports of extensive cavitation occurring in broncho-alveolar cell carcinoma.^{15,16}

Metastatic tumors with roentgenographic cavitation are more evenly distributed between squamous cell (44%) and adenocarcinoma (36%). Table I shows the cases found in the literature^{2,4,14} indicating sites of origin of these metastases.

There are several explanations offered for the pathogenesis of cavitory tumors. Bronchial obstruction with infection distal to the tumor may lead to lung abscess. However, Chaudhuri⁴ could find only three cases in a series of 25 that had identifiable communication with the bronchial tree. However, all of his cases had extensive vascular invasion and 14 cases had thromboses as well. Chaudhuri considered that cavitation results from the tumor outgrowing its blood supply, destruction of vessels by tumor, or plugging of vessels by tumor thrombi. Since the vascular supply is richest at the margins of metastases, central ischemia leads to necrosis and cavity formation.⁴

Another possible mechanism for

cavitation is desquamation and liquefaction within the tumor mass. Dodd and Boyle² attributed this phenomenon to the inherent properties of squamous epithelium. When stratified epithelium is exposed to air, the surface cells dehydrate and fuse to form a protective layer of keratin. As deeper cells reproduce, new cells are pushed to the surface and the older cells are sloughed. These authors suggest that the same process occurring in the center of a neoplastic mass in the absence of air could result in a semiliquid substance producing a cavity appearance on x-ray.²

Another concept recently propounded is "cell autophagism".⁶ This is based on the idea that enzymatic systems inherent in the tumor cells provoke continuous autolysis of the neoplasm.

Summary

A case report of excavating pulmonary metastases from a primary carcinoma of the esophagus is presented. Cavitation in tumors metastatic to the lung are not extremely rare. Explanations of the cavitation include 1) obstruction of airways with subsequent infection; 2) loss of vascular supply; 3) desquamation and liquefaction within squamous cell tumors and 4) cell autophagism.

References

1. LaFORET, E. AND LaFORET, M.: Non-tuberculous cavitory disease of the lungs, *Dis. Chest*, 1957, 31, 655.
2. DODD, G. AND BOYLE, J.: Excavating pulmonary metastases, *Amer. J. Roentgen.*, 1961, 85, 277.
3. LeMAY, M. AND PIRO, A.: Cavitory pulmonary metastases, *Ann. Int. Med.*, 1965, 62, 59.
4. CHAUDHURI, M.: Cavitory pulmonary metastases, *Thorax*, 1970, 25, 375.
5. BERGER, M. AND THOMPSON, J.: Cavitory carcinomatosis of the lungs, *Dis. Chest*, 1967, 52, 106.

TABLE I: Site of Origin of Cavitating Pulmonary Metastases

Cell Type	Site of Primary	No. Cases
Squamous Cell	Female genitalia	15
	Pharynx and Larynx	9
	Opposite lung	7
	Tongue and epiglottis	2
	Bladder	2
	Esophagus	1
	Penis	1
	Anal canal	1
Unknown	3	
		42 (44%)
Adenocarcinoma	Colon, rectum	20
	Stomach	2
	Breast	2
	Pancreas	4
	Breast and pancreas	5
	Kidney	1
		34 (36%)
Others		
Alveolar cell	Opposite lung	1
Hypernephroma	Kidney	1
Transitional cell carcinoma	Bladder	3
Undifferentiated carcinoma	Unknown	1
Seminoma	Testes	1
Teratocarcinoma	Mediastinum	1
Sarcoma	Unknown	2
Osteogenic sarcoma	Bone	6
Wilm's tumor	Kidney	2
Angiosarcoma	Buttock	1
		19 (20%)
TOTAL		95 (100%)

14. COUSSEMENT, A. AND GOODING, C.: Cavitating pulmonary metastatic disease in Children, *Amer. J. Roentgen. Rad. Ther. and Nuc. Med.*, 1973, 117, 833.
15. WORMER, D.: Cavitory bronchiolar carcinoma. *Amer. Rev. Resp. Dis.*, 1969, 99, 773.
16. OHBA, S., TAKASHIMA, T. AND HAMADA, S.: Multiple cystic cavitary alveolar cell carcinoma, *Radiology*, 1972, 104, 65.
17. CHAUDHURI, M.: Primary pulmonary cavitating carcinomas, *Thorax*, 1973, 28, 354.

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6. ZORINI, A.: Primary carcinomatosis cavities of the lungs; Possible role of neoplastic cell autophagism, *Dis. Chest*, 1967, 52, 329.
7. LEHAR, T., CARR, D., MILLER, W., PAYNE, W. AND WOOLNER, L.: Roentgenographic appearance of bronchogenic adenocarcinoma, *Amer. Rev. Resp. Dis.*, 1967, 96, 245.
8. BYRD, R., MILLER, W., CARR, D., PAYNE, W. AND WOOLNER, L.: The roentgenographic appearance of squamous cell carcinoma of the bronchus. *Mayo Clin. Proc.*, 1968, 43, 327.
9. BYRD, R., MILLER, W., CARR, D., PAYNE, W. AND WOOLNER, L.: The roentgenographic appearance of large cell carcinoma of the bronchus. *Mayo Clin. Proc.*, 1968, 43, 333.
10. BYRD, R., MILLER, W., CARR, D., PAYNE, W. AND WOOLNER, L.: The roentgenographic appearance of small cell carcinoma of the bronchus, *Mayo Clin. Proc.*, 1968, 43, 337.
11. STRANG, C. AND SIMPSON, J.: Carcinomatous abscess of the lung, *Thorax*, 1953, 8, 11.
12. COHEN, S. AND HOSSAIN, M.: Primary carcinoma of the lung, *Dis. Chest*, 1966, 49, 67.
13. EMERSON, G., EMERSON, M. AND SHERWOOD, C.: The natural history of carcinoma of the lung, *J. Thoracic Surg.*, 1959, 37, 291.

PRESCRIBING INFORMATION
Antiminth (pyrantel pamoate) Oral Suspension

Actions. Antiminth (pyrantel pamoate) has demonstrated anthelmintic activity against *Enterobius vermicularis* (pinworm) and *Ascaris lumbricoides* (roundworm). The anthelmintic action is probably due to the neuromuscular blocking property of the drug.

Antiminth is partially absorbed after an oral dose. Plasma levels of unchanged drug are low. Peak levels (0.05-0.13 µg/ml.) are reached in 1-3 hours. Quantities greater than 50% of administered drug are excreted in feces as the unchanged form, whereas only 7% or less of the dose is found in urine as the unchanged form of the drug and its metabolites.

Indications. For the treatment of ascariasis (roundworm infection) and enterobiasis (pinworm infection).

Warnings. *Usage in Pregnancy:* Reproduction studies have been performed in animals and there was no evidence of propensity for harm to the fetus. The relevance to the human is not known.

There is no experience in pregnant women who have received this drug.

Precautions. Minor transient elevations of SGOT have occurred in a small percentage of patients. Therefore, this drug should be used with caution in patients with pre-existing liver dysfunction.

Adverse Reactions. The most frequently encountered adverse reactions are related to the gastrointestinal system.

Gastrointestinal and hepatic reactions: anorexia, nausea, vomiting, gastralgia, abdominal cramps, diarrhea and tenesmus, transient elevation of SGOT.

CNS reactions: headache, dizziness, drowsiness, and insomnia. Skin reactions: rashes.

Dosage and Administration. *Children and Adults:* Antiminth Oral Suspension (50 mg. of pyrantel base/ml.) should be administered in a single dose of 11 mg. of pyrantel base per kg. of body weight (or 5 mg./lb.); maximum total dose 1 gram. This corresponds to a simplified dosage regimen of 1 cc. of Antiminth per 10 lb. of body weight. (One teaspoonful = 5 cc.)

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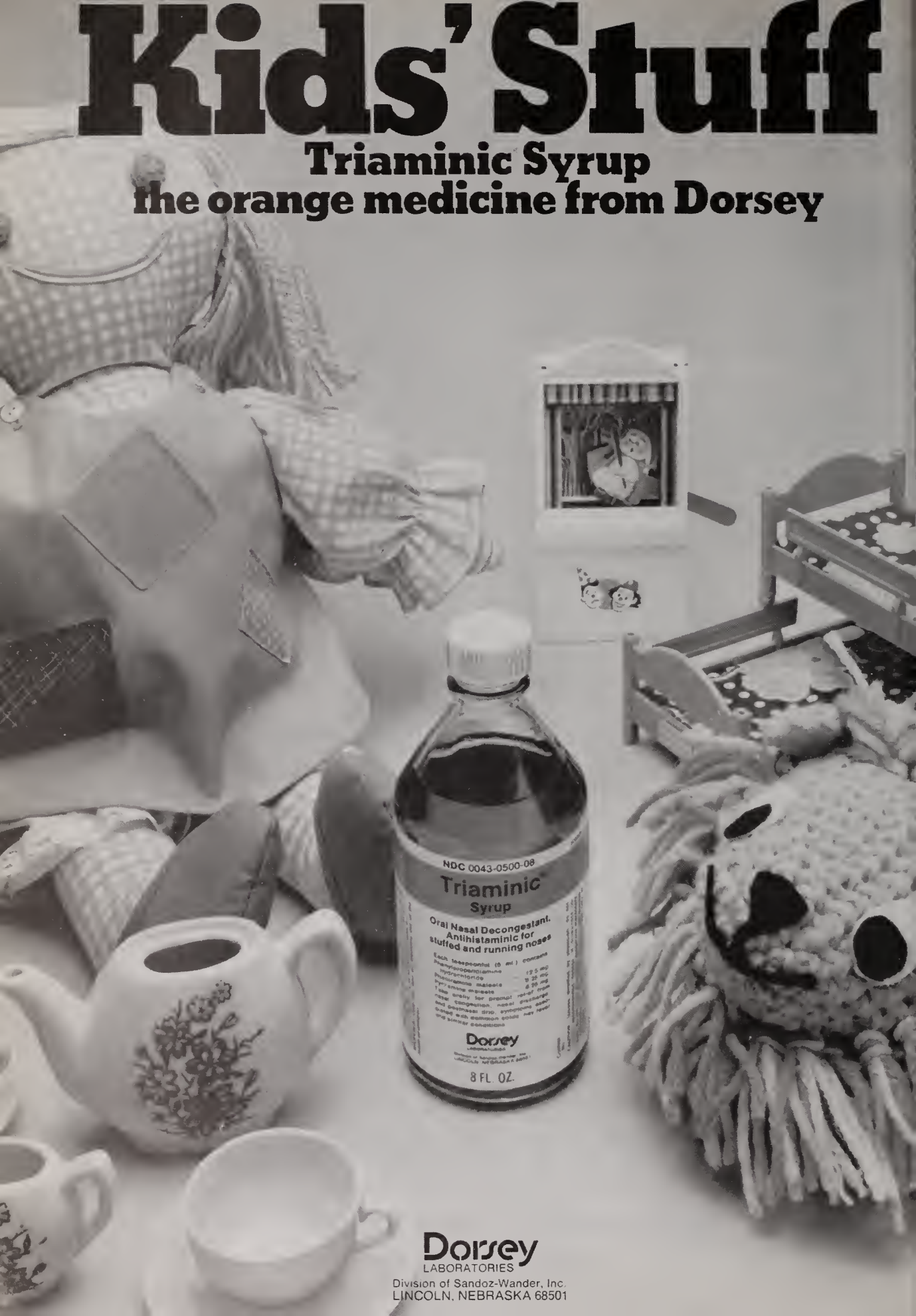
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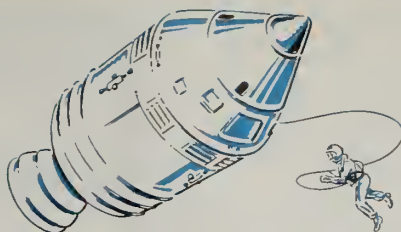
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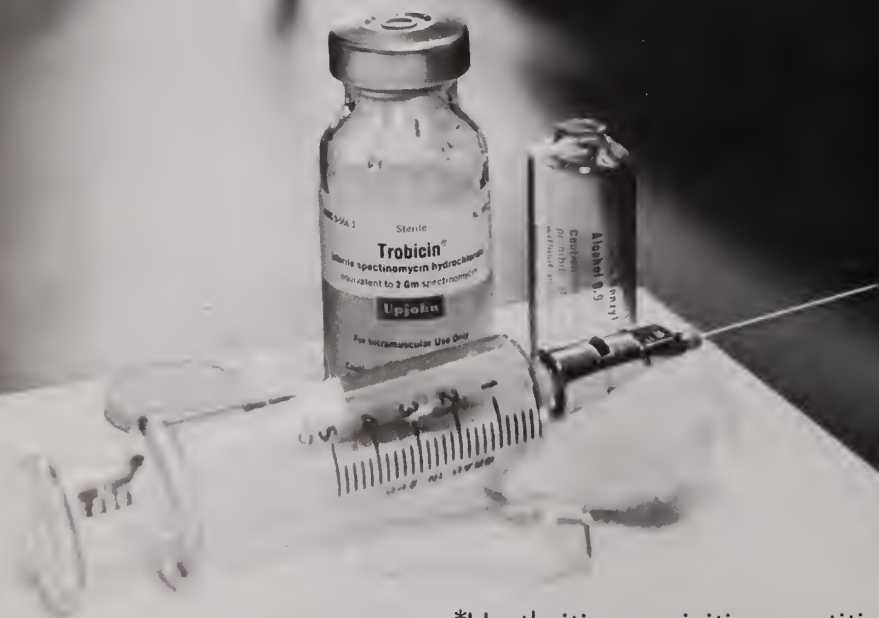
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Contraindications: Contraindicated in patients previously found hypersensitive to spectinomycin.

Warnings: Not indicated for the treatment of syphilis. Antibiotics used to treat gonorrhea may mask or delay the symptoms of incubating syphilis. Patients should be carefully examined and monthly serological follow-up for at least 3 months should be instituted if the diagnosis of

syphilis is suspected.

Safety for use in infants, children and pregnant women has not been established.

Precautions: The usual precautions should be observed with atopic individuals. Clinical effectiveness should be monitored to detect evidence of development of resistance by *N. gonorrhoeae*.

Adverse reactions: The following reactions were observed during the single-dose clinical trials: soreness at the injection site, urticaria, dizziness, nausea, chills, fever and insomnia. During multiple-dose subchronic tolerance studies in normal human volunteers, the following were noted: a decrease in hemoglobin, hematocrit and creatinine clearance; elevation of alkaline phosphatase, BUN and SGPT. In single- and multiple-dose studies in normal volunteers, a reduction in urine output was noted. Extensive renal function studies demonstrated no consistent changes indicative of renal toxicity.

Dosage and administration: Keep at 25° C and use within 24 hours after reconstitution with diluent.

Male—Inject 5 ml intramuscularly for a 2 gram dose. Patients with gonorrheal proctitis and patients being re-treated after failure of previous antibiotic therapy should receive 4 grams (10 ml). In geographic areas where antibiotic resistance is known to be prevalent, initial treatment with 4 grams (10 ml) intramuscularly is preferred.

Female—Inject 10 ml intramuscularly for a 4 gram dose.

How supplied: Vials, 2 and 4 grams—with ampoule of Bacteriostatic Water for Injection with Benzyl Alcohol 0.9% w/v. Reconstitution yields 5 and 10 ml respectively with a concentration of 400 mg spectinomycin per ml (as the hydrochloride). For intramuscular use only. **Susceptibility Powder**—for testing *in vitro* susceptibility of *N. gonorrhoeae*.

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Precautions: Exercise caution in: moderate to severe hepatic disease; anticoagulant therapy, because of possible increased metabolism of coumarin anticoagulants; withdrawal in drug dependence or the taking of excessive doses over a long period, to avoid withdrawal symptoms; elderly or debilitated patients, to avoid possible marked excitement or depression; use with alcohol or other CNS depressants, because of combined effects.

Adverse Reactions: Slight hangover, drowsiness, lethargy, headache, skin eruptions, nausea and vomiting, hypersensitivity reactions (especially in those with asthma, urticaria, angioneurotic edema, or similar conditions).

Usual Adult Dosage: For daytime sedation, 15 mg. to 30 mg. t.i.d. or q.i.d. For hypnosis, 50 mg. to 100 mg.

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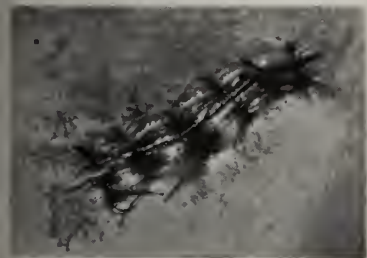
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* **Indications:** Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indication as follows:

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Final classification of this indication requires further investigation.

Contraindications: Acute intermittent porphyria and allergic or idiosyncratic reactions to carisoprodol or related compounds such as meprobamate, mebutamate, tybamate.

Warnings: *Idiosyncratic Reactions:* Rarely, first dose has been followed by extreme weakness, transient quadriplegia, dizziness, ataxia, temporary vision loss, diplopia, mydriasis, dysarthria, agitation, euphoria, confusion, disorientation. Symptoms usually subside during the next several hours. Supportive and symptomatic therapy, including hospitalization, may be necessary.

Pregnancy and Lactation: Safe use not established; weigh

potential benefits against potential hazards in pregnancy, nursing mothers, or women of childbearing potential.

Children Under Five: Drug not recommended.

Potentially Hazardous Tasks: Driving a motor vehicle or operating machinery.

Additive Effects: Possible additive effects between carisoprodol, alcohol, and other CNS depressants or psychotropic drugs.

Drug Dependence: Use cautiously in addiction-prone patients.

Precautions: To avoid excess accumulation, use caution in patients with compromised liver or kidney function.

Adverse Reactions: *Central Nervous System:* Drowsiness, dizziness, vertigo, ataxia, tremor, agitation, irritability, headache, depressive reactions, syncope, insomnia.

Allergic or Idiosyncratic: Usually seen after 1-4 doses in patient not previously exposed, e.g., rash, erythema multiforme, pruritus, eosinophilia, fixed drug eruption with cross reaction to meprobamate. More severe manifestations: asthma, fever, weakness, dizziness, angioneurotic edema, smarting eyes, hypotension, anaphylactoid shock. Stop drug, treat symptomatically (e.g., possible use of epinephrine, antihistamines, and in severe cases corticosteroids).

Cardiovascular: Tachycardia, postural hypotension, facial flushing.

Gastrointestinal: Nausea, vomiting, hiccup, epigastric distress.

Hematologic: Leukopenia and pancytopenia (on carisoprodol plus other drugs).

Usual Adult Dosage: One 350 mg tablet three times daily and at bedtime.

Overdosage: Has produced stupor, coma, shock, respiratory depression, and, very rarely, death. Overdosage of carisoprodol plus alcohol or other CNS depressants or psychotropic drugs can be additive. Empty stomach, treat symptomatically; cautiously give respiratory assistance, CNS stimulants, pressor agents as needed. Carisoprodol is metabolized in the liver and excreted by the kidney. Diuresis and dialysis have been used successfully with related drug meprobamate. Carefully monitor urinary output; avoid overhydration; observe for possible relapse due to incomplete gastric emptying and delayed absorption.

Before prescribing, consult package circular or latest PDR information.

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Indications: SYNTHROID (sodium levothyroxine) is specific replacement therapy for diminished or absent thyroid function resulting from primary or secondary atrophy of the gland, congenital defect, surgery, excessive radiation, or antithyroid drugs. Indications for SYNTHROID (sodium levothyroxine) **Tablets** include myxedema, hypothyroidism without myxedema, hypothyroidism in pregnancy, pediatric and geriatric hypothyroidism, hypopituitary hypothyroidism, simple (nontoxic) goiter, and reproductive disorders associated with hypothyroidism. SYNTHROID (sodium levothyroxine) **for Injection** is indicated for intravenous use in myxedematous coma and other thyroid dysfunctions where rapid replacement of the hormone is required. The injection is also indicated for intramuscular use in cases where the oral route is suspect or contraindicated due to existing conditions or to absorption defects, and when a rapid onset of effect is not desired.

Precautions: As with other thyroid preparations, an overdosage of SYNTHROID (sodium levothyroxine) may cause diarrhea or cramps, nervousness, tremors, tachycardia, vomiting and continued weight loss. These effects may begin after four or five days or may not become apparent for one to three weeks. Patients receiving the drug should be observed closely for signs of thyrotoxicosis. If indications of overdosage appear, discontinue medication for 2-6 days, then resume at a lower dosage level. In patients with diabetes mellitus, careful observations should be made for changes in insulin or other antidiabetic drug dosage requirements. If hypothyroidism is accompanied by adrenal insufficiency, such as Addison's Disease (chronic adrenocortical insufficiency), Simmonds's Disease (panhypopituitarism) or Cushing's syndrome (hyperadrenalism), these dysfunctions must be corrected prior to and during SYNTHROID (sodium levothyroxine) administration. The drug

should be administered with caution to patients with cardiovascular disease; development of chest pains or other aggravations of cardiovascular disease requires a reduction in dosage.

Contraindications: Thyrotoxicosis, acute myocardial infarction. **Side effects:** The effects of SYNTHROID (sodium levothyroxine) therapy are slow in being manifested. Side effects, when they occur, are secondary to increased rates of basal metabolism; sweating, heart palpitations with or without pain, leg cramps, and weight loss. Diarrhea, vomiting, and nervousness have also been observed. Myxedematous patients with heart disease have died from abrupt increases in dosage of thyroid drugs. Careful observation of the patient during the beginning of any thyroid therapy will alert the physician to any untoward effects.

It has been shown that *Synthroid* (T₄) converts to T₃ at the cellular level to supply metabolic needs.^{1, 2}

1 *Synthroid* is T₄.

2 Because T₄ converts to T₃ at the cellular level, it provides full thyroid replacement at maintenance doses.^{1, 2}

3 T₄ hormone content is controlled by chemical assay.

4 *Synthroid* is assayed chemically; no biologic test is necessary to measure potency.

5 *Synthroid* provides predictable results when used with current thyroid function tests.

6 *Synthroid* is the most prescribed brand name of thyroid in the U.S. and Canada.

7 Sodium levothyroxine in *Synthroid* tablets is chemically pure. It does not contain any animal gland parts.

8 When stored properly, *Synthroid* has a longer shelf life than desiccated thyroids.

9 On a daily basis, *Synthroid* is cost competitive with other thyroid products.

The smooth road to
thyroid replacement therapy.

Synthroid[®]
(sodium levothyroxine)

In most cases with side effects, a reduction of dosage followed by a more gradual adjustment upward will result in a more accurate indication of the patient's dosage requirements without the appearance of side effects.

Dosage and Administration: The activity of a 0.1 mg. SYNTHROID (sodium levothyroxine) TABLET is equivalent to approximately one grain thyroid, U.S.P. Administer SYNTHROID tablets as a single daily dose. In hypothyroidism without myxedema, the usual initial adult dose is 0.1 mg. daily, and may be increased by 0.1 mg. every 30 days until proper metabolic balance is attained. Clinical evaluation should be made monthly and PBI measurements about every 90 days. Final maintenance dosage will usually range from 0.2-0.4 mg. daily. In adult myxedema, starting dose should be 0.025 mg. daily. The

dose may be increased to 0.05 mg. after two weeks and to 0.1 mg. at the end of a second two weeks. The daily dose may be further increased at two-month intervals by 0.1 mg. until the optimum maintenance dose is reached (0.1-1.0 mg. daily).

Supplied: Tablets: 0.025 mg., 0.05 mg., 0.1 mg., 0.15 mg., 0.2 mg., 0.3 mg., 0.5 mg., scored and color-coded, in bottles of 100, 500, and 1000. Injection: 500 mcg. lyophilized active ingredient and 10 mg. of Mannitol, U.S.P., in 10 ml. single-dose vial, with 5 ml. vial of Sodium Chloride Injection, U.S.P., as a diluent. SYNTHROID (sodium levothyroxine) for Injection may be administered intravenously utilizing 200-400 mcg. of a solution containing 100 mcg. per ml. If significant improvement is not shown the following day, a repeat injection of 100-200 mcg. may be given.

1. Braverman, L. E., Ingbar, S. H., and Sterling, K.: Conversion of Thyroxine (T₄) to Triiodothyronine (T₃) in Athyreotic Human Subjects, *J. Clin. Invest.* 49:855-64, 1970.

2. Surks, M. I., Schadow, A. R., and Oppenheimer, J. H.: A New Radioimmunoassay for Plasma L-Triiodothyronine: Measurements in Thyroid Disease and in Patients Maintained on Hormonal Replacement. *J. Clin. Invest.* 51:3104-13, 1972.



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BS-RD

POST GRADUATE EDUCATION

MEDICAL MANAGEMENT OF RHEUMATOID ARTHRITIS

Anthony J. Sliwinski, M.D.

The management of rheumatoid arthritis includes rest, physical medicine, non-specific anti-inflammatory drugs, analgesics, anti-rheumatic drugs, intraarticular steroids, cytostatic drugs and surgery. The choice of therapy must be individualized for each patient. No one program is always successful; hence, there must be constant re-evaluation of therapy with appropriate changes as needed. This discussion will be limited to drug therapy, recognizing that all patients need at least some physical medicine even if it is only a simple home program.

The most useful non-specific anti-inflammatory drug is aspirin in large, regular doses. It must be stressed to the patient that aspirin (ASA) is being used to suppress inflammation and not as an analgesic. Therefore, it should be taken as 5 grain tablets with each meal and 4 tablets at bedtime with food, milk or antacids. If the patient develops GI distress on ordinary aspirin, Ascriptin (aspirin with Maalox), Ecotrin (enteric coated ASA), or Arthropan (cholisalicylate, 1 tsp = 10 grains), may be tried. Patients allergic to aspirin may be treated with sodium salicylate. The dose is gradually increased until the desired effect is obtained or the patient develops salicylism. The earliest signs of aspirin intoxication include deafness and tinnitus. Salicylate levels $2\frac{1}{2}$ to 3 hours after a dose of aspirin should be between 15 mgm and 25 mgm percent. Occasional patients cannot tolerate aspirin in any form. In this situation, aspirin substitutes such as Indomethacin or Phenylbutazone may be used. Acetaminophen is not a useful drug for the treatment of rheumatoid arthritis since it lacks anti-inflammatory properties and is a pure analgesic antipyretic drug.

Indomethacin is associated with occasional gastrointestinal intolerance and central nervous system side effects, particularly in elderly patients. These side effects may be minimized if the drug is started at a low dose and gradually increased. The usual method is to start with 25 mgm at lunchtime, and 25 mgm at bedtime with food, milk or antacid. After 3-5 days, it is increased to 3 capsules a day,

then to 4 capsules a day. If there is suboptimal improvement, the evening dose may be increased to 50 mgm as well as the a.m. dose. Phenylbutazone and its analog Oxyphenylbutazone, is given in a dose of 200 mgm to 400 mgm a day. Again, because of its gastrointestinal toxicity it should be given only with meals, milk or antacid. However, these drugs have two additional potential side effects that require caution in their use. They may induce bone marrow suppression so that frequent CBC's need to be monitored while the patient is on the drug, and they also may cause some degree of sodium retention. In elderly patients with cardiac disease they may be sufficient to induce congestive heart failure. Corticosteroids in small doses are useful adjuncts to the non-specific anti-inflammatory drugs. However, they are used to only reduce some of the symptoms and not to completely control the disease. Hence, the dose of Prednisone is limited to no more than 10 mgm a day in men and to no more than 7.5 mgm a day in women.

There are two anti-rheumatic drugs available: antimalarial drugs and soluble gold salts. Both of these agents have in common a 6 to 16 week lag period from institution of therapy to clinical improvement. The antimalarial drugs are easiest to give; however, they are associated with a serious complication; that is, macular damage that can lead to blindness.

The antimalarial drug easily available is Hydroxychloroquine 200 mgm tablets. The usual dose is 400 mgm a day for six weeks. The patient is then re-evaluated and if there is clinical improvement, the dose is reduced to 200 mgm a day. Thereafter, the patient is repeatedly evaluated with continued attempts at keeping the dose at the lowest level possible to maintain control of the disease. Antimalarial drugs bind to the melanin pigments, making the retina susceptible to the injurious effects of bright light. Hence, the use of sunglasses out of doors may help reduce this hazard. In addition, it is mandatory that all patients on these drugs have

POST-GRADUATE EDUCATION

frequent ophthalmologic examinations to detect early changes of antimalarial damage. If changes are found, the drug should be discontinued promptly and probably permanently. The ophthalmologist should not only visualize macula but in addition do visual fields using a 2 mm red target, since it would seem that changes in visual field pre-date the appearance of pigmentary changes. In selected cases, fluorescein angiography may be a useful adjunct to detect early damage. There is an additional ocular toxicity—that of corneal deposits which are rather benign and always disappear with cessation of therapy and, in fact, may even disappear with continued therapy.

Two soluble gold salts are commonly used in the management of rheumatoid arthritis, gold thiomalate and gold thioglucose. The major side effects of gold therapy include an allergic skin rash, bone marrow suppression, and proteinuria. The usual program consists of a 5 mgm test dose followed by 15 mgm in one week, and 25 mgm the second week. Thereafter, weekly doses of 25 mgm or 50 mgm may be administered until a total of 12-16 doses have been received by the patient. At that point in time, if the patient is improving, the interval between injections may be increased to two weeks for four injections,

and then three week intervals for four injections, and then every four weeks thereafter. Before each injection of gold, it is necessary that the patient be checked for the appearance of a skin rash, blood count obtained, and urine tested for protein. If any toxicity is present, the medication should be discontinued and rarely, if ever, re-instituted. If relapse occurs during treatment, the patient may be again treated with weekly gold injections for 6-12 doses or until the disease is brought under control and the interval again slowly increased. Many patients require every 2-3 week therapy and cannot be increased to every four weeks.

The use of cytostatic drugs (cyclophosphamide and chlorambucil) and D-penicillamine are at the present time experimental. They are currently the most effective method for controlling severe rheumatoid disease but have potential hazardous side effects and should probably be reserved for use only under research conditions.

Anthony J. Sliwinski, M.D. is Assistant Professor of Medicine, Georgetown University Medical School, Washington, D.C.

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The more physicians consider the hemodynamics of lowering blood pressure...

Most physicians now agree on the importance of reducing blood pressure in the hypertensive patient. But high blood pressure exists, of course, only as part of a complete clinical picture. The hemodynamic profile of well-established essential hypertension is characterized by elevated arterial blood pressure, normal cardiac output, and increased total peripheral resistance.

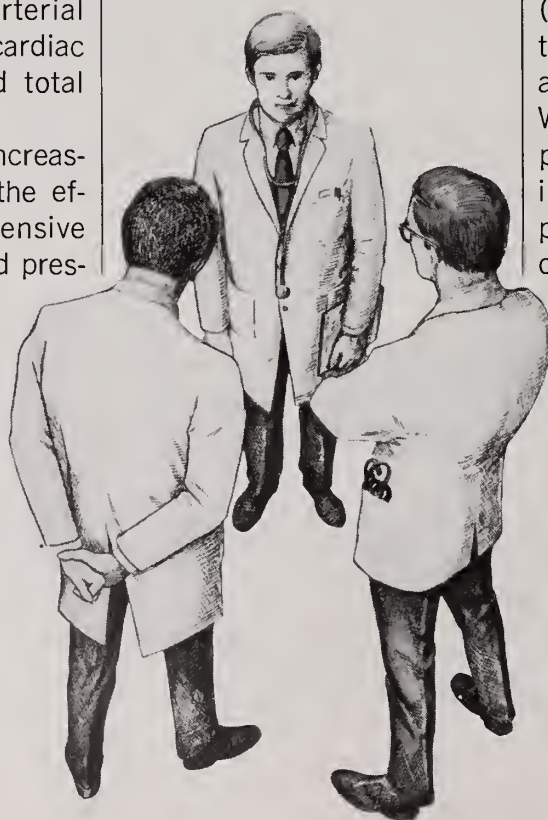
And so, physicians are increasingly concerned with the effects of an antihypertensive agent not only on blood pres-

sure itself but also on the hemodynamic pattern—in short, with the total effect of the drug. *Does it indeed help lower blood pressure effectively? Is peripheral resistance reduced? Are cardiac output and renal functions main-*

tained? And, also, is there likely to be drug-induced postural hypotension serious enough to pose a threat to the patient's cerebrovascular status?

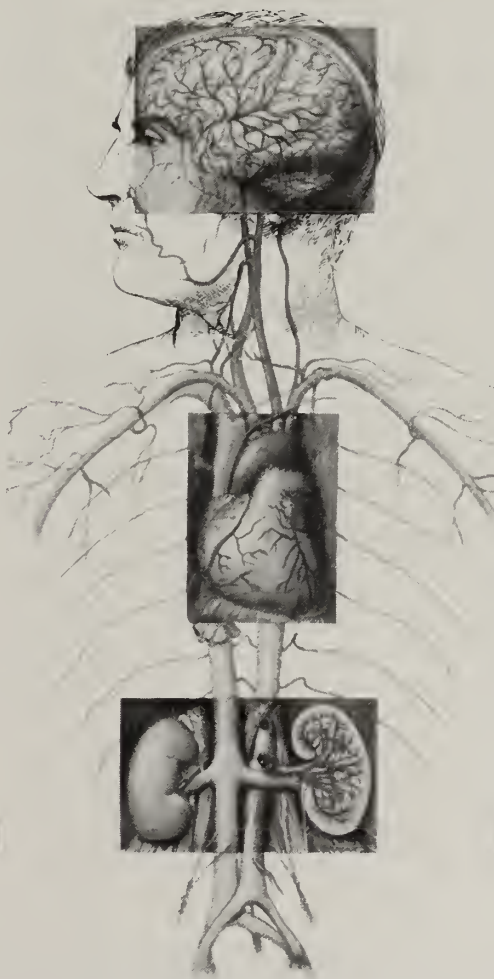
With this emphasis on overall drug performance has come a growing reliance on ALDOMET® (Methyldopa, MSD) in the treatment of sustained moderate hypertension.

With its unique hemodynamic profile, ALDOMET has drawn increasing attention and approval from physicians. First, of course, for its efficacy in



the more physicians rely on this unique antihypertensive

lowering blood pressure. But there are other considerations as well. Cardiac output is usually maintained with no cardiac acceleration; in some patients the heart rate is actually slowed. Peripheral resistance is apparently reduced. ALDOMET does not usually compromise existing renal function; it generally does not reduce renal blood flow, glomerular filtration rate, or filtration fraction. And ALDOMET usually does not cause symptomatic postural or exercise hypotension.



Some patients on continuous methyldopa therapy may develop a positive direct Coombs test. For more details, see the brief summary of prescribing information.

Contraindicated in active hepatic disease and known sensitivity to the drug. Not recommended in pheochromocytoma or pregnancy. It should be used with caution in patients with a history of liver disease or dysfunction. Discontinue the drug if fever, abnormal liver function, jaundice, or acquired hemolytic anemia occurs.

In most cases of sustained moderate hypertension

TABLETS, 250 mg

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(METHYLDOPA | MSD)

smoothly lowers blood pressure

For a brief summary of prescribing information, please see following page.

In most cases of sustained moderate hypertension

TABLETS, 250 mg

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smoothly lowers blood pressure

Contraindications: Active hepatic disease, such as acute hepatitis and active cirrhosis; known sensitivity. Not recommended in pheochromocytoma. Unsuitable in mild or labile hypertension responsive to mild sedation or thiazide therapy. Use cautiously in patients with history of previous liver disease or dysfunction.

Warnings: Acquired hemolytic anemia has occurred rarely in association with therapy with methyldopa. Should clinical symptoms indicate the possibility of anemia, hemoglobin and/or hematocrit determinations should be performed. If anemia is present, appropriate laboratory studies should be done to determine if hemolysis is present. Evidence of hemolytic anemia is an indication for discontinuation of the drug. Discontinuation of methyldopa alone or the initiation of adrenocortical steroids usually results in a prompt remission of the anemia. Rarely, however, fatalities have occurred.

Some patients on continued therapy with methyldopa develop a positive direct Coombs test; incidence reported has averaged between 10% and 20%. It rarely occurs in first six months of therapy, and if not seen within twelve months, is unlikely to develop with continued administration. Positive Coombs test is dose-related; lowest incidence occurs in patients on 1 g methyldopa or less per day. Reversal of the positive Coombs test occurs within weeks to months after discontinuation of methyldopa. Prior knowledge of a positive Coombs reaction aids in evaluation of cross match for transfusions. Patients with positive Coombs tests at time of cross match may exhibit incompatible minor cross match. When this occurs, an indirect Coombs test should be performed. If negative, transfusion with blood otherwise compatible in the major cross match may be carried out. If positive, advisability of transfusion with blood compatible in major cross match should be determined by hematologist or expert in transfusion problems.

Fever has occurred within first three weeks of therapy, sometimes with eosinophilia or abnormalities in liver function tests, such as serum alkaline phosphatase, serum transaminases (SGOT, SGPT), bilirubin, cephalin cholesterol flocculation, prothrombin time, and bromsulphalein retention. Jaundice, with or without fever, may occur, with onset usually in the first two to three months of therapy. Rare cases of fatal hepatic necrosis have been reported. Liver biopsy in several patients with liver dysfunction has shown microscopic focal necrosis compatible with drug hypersensitivity. Rarely, reversible reduction in leukocyte count with primary effect on granulocytes has been seen; reversible agranulocytosis has been reported. Methyldopa may interfere with measurement of creatinine by alkaline picrate method and of uric acid by photungstate method. When used with other antihypertensive drugs, potentiation of antihypertensive action may occur.

Usage in Pregnancy and Childbearing Age—Not

recommended in pregnancy. In women of childbearing age, weigh potential benefits against possible fetal hazards.

Precautions: Perform periodic hepatic function tests and white cell and differential blood counts during first six to twelve weeks of therapy or in unexplained fever. Discontinue if fever, abnormalities in liver function tests, or jaundice appears. Since methyldopa causes fluorescence in urine samples at the same wavelengths as catecholamines, spuriously high levels of urinary catecholamines may be reported. This will interfere with the diagnosis of pheochromocytoma. Discontinue drug if involuntary choreoathetotic movements occur in patients with severe bilateral cerebrovascular disease. Anesthetics requirements may be reduced; hypotension occurring during anesthesia usually can be controlled with vasopressors. Hypertension may occur after dialysis because methyldopa is removed by this procedure.

Dosage should be limited initially to 500 mg daily when following previous antihypertensive agents other than thiazides. Do not exceed recommended daily dose of 3.0 g. Patients with impaired renal function may respond to smaller doses than patients with normal kidney function. Syncope in older patients has been related to increased sensitivity in those with advanced arteriosclerotic vascular disease; this may be avoided by lower doses. Tolerance occasionally seen either early or late, but more likely between second and third month after initiation of therapy; increased dosage or combined therapy with a thiazide frequently restores effective control.

Adverse Reactions: Sedation, usually transient, may be seen during initial therapy or when dosage is increased. Headache, asthenia, or weakness may be noted as early, transient symptoms. Symptoms associated with effective lowering of blood pressure, including dizziness, lightheadedness, and symptoms of cerebrovascular insufficiency, are seen occasionally. Angina pectoris may be aggravated. Symptoms of orthostatic and exercise hypotension may occur; if symptoms occur, reduce dosage. Bradycardia, nasal stuffiness, mild dryness of mouth, and gastrointestinal symptoms including distension, constipation, flatus, and diarrhea occur occasionally; these can be relieved by reducing dosage. Nausea and vomiting have been reported in only a few patients. Sore tongue or "black tongue," pancreatitis, and inflammation of salivary glands may occur.

Weight gain and edema occur infrequently; if edema progresses or signs of pulmonary congestion appear, discontinue drug. Rarely, urine exposed to air may darken due to breakdown of methyldopa or its metabolites. Other rare reactions include breast enlargement, lactation, impotence, decreased libido, skin rash, mild arthralgia, myalgia, paresthesias, parkinsonism, psychic disturbances including nightmares, reversible mild psychoses or depression, reversible thrombocytopenia, drug-related fever and abnormal liver function studies with jaundice and hepatocellular damage (see **Warnings** and **Precautions**), rise in BUN, and a single case of bilateral Bell's palsy.

Supplied: Tablets, containing 250 mg methyldopa each, in single-unit packages of 100 and bottles of 100 and 1000.

For more detailed information, consult your MSD representative or see full prescribing information. Merck Sharp & Dohme, Division of Merck & Co., INC., West Point, Pa. 19486

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ADDENDUM

Let's make blood pressure "required reading" for all physicians.

With recent estimates that about 23 million Americans have high blood pressure—and that half of them are not even aware of it—detection of the problem in asymptomatic persons has become an issue of national importance.

Family physicians are being urged to take blood pressure readings as a matter of office routine, regardless of the presenting complaint or the reason for the visit. And because many people do not see a family physician for relatively long periods of time, some experts are suggesting that ophthalmologists, gynecologists, dermatologists, orthopedists, psychiatrists, dentists, school nurses, family planning counselors, and other health-care personnel make blood pressure reading a routine part of every examination or consultation.

Of course, a diagnosis of hypertension cannot be made on the basis of a single reading, but routine blood pressure readings can uncover potential trouble in a certain proportion of patients. And when trouble is suggested, further evaluation can be pursued more effectively.



Blood pressure—
"required reading"
for all physicians

BOOK REVIEWS

Pharmacology—Drug Actions and Reactions.

RUTH R. LEVINE, Ph.D. Price, \$14.50. Pp. 412.
Boston, Massachusetts: Little, Brown and Company,
1973.

There is a substantial amount of fundamental information that is pertinent to the understanding of the interaction between drugs and the living organism. This information consists of the principles governing transfer of drugs from the site of administration to the locus of action, and ultimately, to the manner in which the action is terminated. It also consists of quantitative aspects of drug action, that is, dose-response relationships and time-response relationships. This information should be a primary thrust of any basic course in pharmacology. Without it, physicians and dentists are severely handicapped in their attempts to use pharmacologically active chemicals as therapeutically effective drugs. Surprisingly, standard textbook treatment of the subject is usually inadequate as both Goodman and Gilman and Drill do not provide a comprehensive, understandable coverage of pharmacologic principles. The purpose of *Pharmacology—Drug Actions and Reactions* by Ruth R. Levine, Ph.D., is just that—i.e., "to provide a concise source of that core of pharmacologic knowledge that can be shared by all wishing to acquire an understanding of how chemical agents affect living processes." The result of Doctor Levine's efforts is impressive. Her book is well written, easy to read, and the information can be readily comprehended. This is largely due to the logical presentation, the definition of terms before they are used, the introductory remarks at the beginning of the sections, and the excellent choice and use of examples to highlight important points and concepts. In addition to providing the fundamental concepts governing drug-tissue interactions, the book also contains chapters on: (1) factors that are responsible for the variability that exists in the response of different individuals to drugs, (2) drug toxicity, (3) development and evaluation of new drugs, and (4) historical development of pharmacology as a science. The material in these chapters reinforces and enlarges upon the basic principles described in the main part of the book.

There are two other textbooks that focus on the principles and mechanisms that are fundamental to the understanding of drug action. These are *Introduction to General Pharmacology* by T. Z. Csáky, and *Principles of Drug Action* by A. Goldstein, L. Aronow, and S. M. Kalman. The first is a brief introductory text while the second is an

extensive detailed analysis of the subject. Doctor Levine's book lies somewhere between the two. As such it is an ideal text to either supplement lectures in General Pharmacology or to even provide the entire learning experience in this area.

This is not a book that will be useful to the individual seeking information about a specific drug. No systematic attempt has been made to discuss either the effects of drugs on various tissues of the body, or the effects of drugs in the treatment of specific diseases. Drugs that are discussed are included for the purpose of illustrating a basic principle.

On the negative side, there are sections dealing with the anatomy and physiology of the kidney and the central nervous system. No real purpose is served by inclusion of this information as the points made can be easily understood without the distraction of these extraneous details. Likewise, there is a chapter on drug abuse and drug dependence that is completely out of place in a text of this type. The content of the chapter has little to do with general principles of pharmacology and I suspect has been added to give the book a wider audience appeal.

RICHARD GILLIS, Ph.D.

Malnutrition—Its Causation and Control. Volumes I and II. JOHN K. ROBSON. Price, two volume set: \$24.50. Vol. I—\$14.95, Vol. II—\$14.95. Pp. 613 with illustrations. New York: Gordon and Breach, Science Publishers, Inc., 1972.

This set of books is written for physicians and public officials who are involved in programs to improve the nutrition in specific population groups. It is not written for physicians who are concerned with metabolics status of individual patients.

In this day of food fadism and widespread misinformation about food, it is refreshing to find a text that is scientifically accurate. Because nutritional requirements are affected by environment, exercise, chronic disease and parasitic infections, one cannot use the same basic nutritional requirements for all population groups.

References to recent literature are adequate and wide gaps in our present knowledge in nutrition are pointed out. This book is a good reference for persons concerned with the nutrition in large groups. JAMES M. MOSS, M.D.

BOOK REVIEWS

Neuro-Ophthalmology, Volume VII. J. LAWTON SMITH AND JOEL S. GLASER. Price, \$22.50. Pp. 146. St. Louis, Missouri: C. V. Mosby Company, 1973.

This book is clearly edited for the practicing physician. Drs. Smith and Glaser have organized this slender volume so that it is incisive and practical. The preface is interesting in itself. A check list of important current points in neuro-ophthalmology is presented. In this are many pearls as well as much helpful advice. The text is dominated by several articles that present broad coverage of well selected topics. Dr. Lubow does a very good job in summarizing edemas of the optic disc. Anyone who ever deals with papilledema, be he internist, neurologist, ophthalmologist, neurosurgeon or pediatrician, will appreciate this chapter. Optic neuropathies due to deficiencies and toxic causes are treated generously by Dr. Lessell. A particularly good discussion is given by Dr. Burde on ischemic optic neuropathy. The pathophysiology of this problem is reviewed nicely. A chapter on microvascular surgery is presented showing general techniques. This will be new to most ophthalmologists but well worth while. Frequently the ophthalmologist is the first to suggest occlusive disease of the carotid artery. We would do well to know more about the surgical corrections done by the vascular surgeons after the diagnosis is made.

In the final chapter of the book Dr. Glaser has edited papers and discussions that were presented during a free-paper session. This chapter is spirited and well worth reading. The contributors to the book and the participants in the discussions represent some of the foremost neuro-ophthalmologists in the country. Neuro-ophthalmology Volume VII is stimulating, informative and recommended. DAVID K. BERLER, M.D.

Hamilton Bailey's Demonstrations of Physical Signs in Clinical Surgery. ALLEN CRAIN, EDITOR. Price, \$33.25. Pp. 620 with illustrations. Baltimore, Maryland: The Williams and Wilkins Company, 1973.

After fifteen editions in English and thirteen in other languages this book retains its position as *the* authority on Surgical Physical Diagnosis. The changes in format are virtually nil, many of the pictures are the same and only a few new concepts have been added by the new editor, Allan Crain.

But what an unusual book it is! There are six hundred and twenty pages, nine hundred and forty-nine illustrations. The writing is vivid and concise. Why can't American writers construct such simple and informative sentences as "Flex the elbow to better palpate a supratrochlear lymph node" or "The umbilicus is a creek into which one of the many fistulous streams can be diverted?"

The photographs selected from a world wide list of contributors are well chosen to illustrate the physical signs and have a nostalgic quality of their own. The poor little girl who demonstrates tuberculosis of the hip must now be an old lady.

The footnotes identify those honored by eponyms and are helpful, sometimes amusing, and only occasionally inaccurate. The index is large and well organized, just the thing for those of us who can never straighten out the hordeolum-chalazion controversy.

In short, this is an undoubted classic, indispensable for the student, and a complete reference for the practicing surgeon. The old cliché "should be in every surgeon's library," is certainly applicable. The changes from previous editions are too small to justify purchase of a new edition if you already have one of the old.

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so-called "senile" keratoses...
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INDEX TO ADVERTISERS

Insurance

Corroon & Black, Russell, Inc.	6
Ralph W. Lee & Company	T-219
Mutual of Omaha	4

Nurse Registries

District of Columbia Manpower Administration	T-230
---	-------

Nutrition Education

Dairy Council of Greater Metropolitan Washington, D.C.	2
--	---

Pharmaceuticals

Abbott Laboratories	T-210
Burroughs Wellcome & Company	T-207, 225
Burton Parsons & Company	T-225
Dorsey Laboratories	T-202, 216
Flint Laboratories	T-214
Eli Lilly & Company	12
McNeil Laboratories	T-206

Merck Sharp &

Dohme Laboratories	T220-222
Pharmaceutical Manufacturers Association	10-11
William P. Poythress & Company	T-203
Reed & Carnrick	T-231
A. H. Robins Company	T-211-212
Roche Laboratories	.000
J. B. Roerig	.000
G. D. Searle & Company	c2, 1, T-226-227, c3, c4
Smith Kline & French Laboratories	9
The Upjohn Company	T-204-205

Pharmacy

Peoples Drug Stores	T-228
---------------------------	-------

Sanitarium

Kalorama Convalescent Home Inc.	T-230
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Therapy

The University Center	T-219
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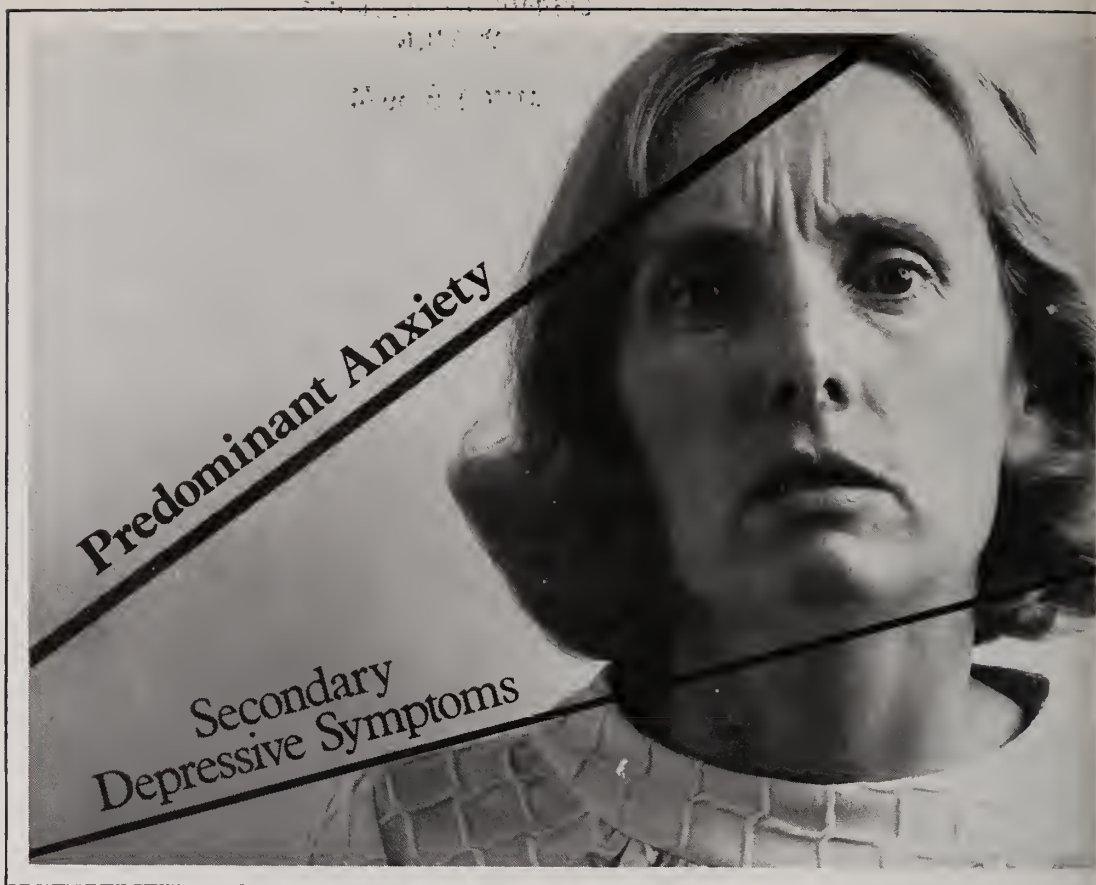
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CONTENTS

SCIENTIFIC ARTICLES

Peripheral Coronary Artery Perfusion for Direct Coronary Artery Reconstruction. Lawrence J. Freant, M.D., Luis A. Mispireta, M.D. and Karel B. Absolon, M.D.	233
Carotid Artery Replacement with a Saphenous Vein Graft for Other Than Arteriosclerotic Obstructive Disease. Kristin Stueber, M.D., Arnaldo A. Garro, M.D. and Karel B. Absolon, M.D.	237
Five Year Followup of Colonic Transplants in Patients with Epidermolysis Bullosa Producing Esophageal Obstruction. Randolph DeLeon, M.D. Luis A. Mispireta, M.D. and Karel B. Absolon, M.D.	241
Tumors of the Heart. Luis A. Mispireta, M.D., H. Brandis Marsh, M.D., James A. Bacos, M.D., Mario H. Diaz, M.D. and Karel B. Absolon, M.D.	245
The Morphology, Physiology and Therapy of Mitral Valve Disease with Giant Left Atria. Anjum G. Qazi, M.D., Luis A. Mispireta, M.D., John V. Russo, M.D., James A. Bacos, M.D. and Karel B. Absolon, M.D.	251
Physiological Rationale for the Clinical Use of Low Output Pacemakers. Nicholas P. D. Smyth, M.D., John M. Keshishian, M.D., Norman R. Baker and Peter Tarjan, Ph.D.	257

OTHER FEATURES

President's Message	5
Some Thoughts About Education. Clifton R. Gruver, M.D.	
Scientific Editorial	7
Anticoagulation III: Anticoagulation and Acute Myocardial Infarction "What the Big Boys Do." James A. Bacos, M.D.	
The View Box	236
Edited by Gunther J. Augustin, M.D.	
ECG Problems	250
Edited by Robert F. Montgomery, M.D.	
Book Reviews	279
Clinical Aspects of Thromboembolism. (Pitney) Reviewed by Bennie A. Moxness, M.A., M.D.	
Rise Up to Life. (Bickel) Reviewed by John G. Stubenbord, M.D.	
Handbook of Ocular Therapeutics and Pharmacology. (Ellis and Smith) Reviewed by Howard N. Bernstein, M.D.	
Information for Authors	282
Advertising and Subscription Information	284
Index to Advertisers	284

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PRESIDENT'S MESSAGE

Some Thoughts About Education

Educators nowadays are in the doldrums. There is a lack of consensus of direction, lack of sufficient funding, and educational programs have overshot. There often are too many chiefs, no Indians. There has been too much attention paid to education per se, and not enough to meeting the needs of society. Six and one half percent of all scientists in this country are unemployed—and not because of recessions. There are 1000 unemployed "Ph.Ds in History." We have been educating too many people for positions which do not exist.

Similar unequal densities have occurred in the medical profession. Our biggest problem area lies in the inadequacy of provision for primary care. The health manpower shortage might not exist if physicians were better distributed.

The graduates of today's medical schools establish in affluent, not deprived or remote, regions. How to attract them into areas of need? What should admission requirements be to provide more family physicians? What should their curriculum be? Can we better utilize women in our profession? How can we achieve greater involvement of the minority groups? Can the National Health Service Corps work? Is there a way of bringing more Public Health Service physicians into the delivery of care? Will the physician's assistant concept come to fruition? These are but a few of the many questions we must address if we are to provide appropriate balance in health needs.

In this century there have been four major trends in medical education. First was the era of general practice, which followed the Flexner report in 1910, ranged to 1940, and in which the emphasis was on the Art of Medicine. Second, came the Age of Specialization, 1940-1959, where the emphasis was directed toward professional competence. Third, an era of Science and Technology (1959 to present) with emphasis on research, hospitals. Finally, today, an Era of Community Medicine where emphasis is placed on delivery, social factors, minority education, etc. These eras have reflected signs of the times relative to the health needs of the nation and the profession itself.

To establish proper balance and direction in our professional education system, and to fulfill the health needs of our country—present and future—we need to combine the thrust of each of these eras—Art, Competence, Science and Need.



CLIFTON R. GRUVER, M.D.
PRESIDENT

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SCIENTIFIC Editorial

ANTICOAGULATION III: ANTICOAGULATION AND ACUTE MYOCARDIAL INFARCTION "WHAT THE BIG BOYS DO"

Webster defines "Editorial" as the rendering of an opinion. Nowhere in medicine is this more applicable than in the use of anticoagulant therapy in acute myocardial infarction. Rather than review the established literature on the subject it seemed more useful to poll the area cardiologists and record their responses. The questions were kept as simple as possible and perhaps, in retrospect, may have been inadequate but they reflected the author's own thoughts with regard to a basis for anticoagulation in acute myocardial infarction.

Thirty-one well-established Internists were contacted. They represented the principal cardiologists of 13 area hospitals and most either are or were directors of Coronary Care Units.

With interpretive comments from the author, the following information was recorded:

Do Washington physicians anticoagulate for acute myocardial infarction?

Twelve physicians answered *yes* and 19 *no*—but all 31 felt that anticoagulation has no salutary effect on the infarct per se and had other reasons for such treatment. This is consonant with published reports that fail to establish a clear difference in mortality between treated and untreated cases.¹

All agreed with anticoagulant prophylaxis for thromboembolism but the basis for such use differed significantly (see Fig. 1).

FIG. 1. Reasons for Prophylactic Anticoagulation in Myocardial Infarction

	Yes	No
1. Size of Infarct	11	20
2. Hypotension or Shock	16	15
3. Congestive Heart Failure	31	
4. Prolonged Rest	27	4
5. Age	14	17
6. Combination of Factors	31	

In regard to infarct size, Wright² in 1954 found mural thrombi in 62% of untreated cases and 32% of treated cases and since it seems logical that the larger the infarct, the bigger the resultant mural thrombus, the disparity in responses was surprising.

Since hypotension and shock are both manifestations of pump failure, either would tend to predispose to thromboembolism but again cardiologists differed significantly.

The question of heart failure clearly evoked a unified response but here again, many physicians required right-sided failure before instituting therapy while others were satisfied with a loud persistent 3rd sound as a basis for treatment.

There was little argument with anticoagulation for prolonged inactivity. This reflects recent studies showing the increased incidence of leg vein thrombosis in acute myocardial infarction.³

Age, too, creates a difference of opinion with many observers being uninfluenced. Others would be prompted to anticoagulate if the patient is relatively young while still others would treat only in the older age groups.

Fig. 2. shows a breakdown of the estimated frequency with which each cardiologist actually anticoagulates in acute infarction.

FIG. 2. Percentage of Patients Anticoagulated In Acute Myocardial Infarction by M.D.

%	# M.D.'s
0-10%	11
11-15%	8
16-20%	1
21-30%	5
31-40%	3
51-60%	1
>60%	2
TOTAL	31

Fully 2/3 of the cardiologists anticoagulate less than two out of 10 patients with acute myocardial infarction. This is an interesting figure and either reflects a too spontaneous and perhaps inaccurate answer or, if true would suggest that very few patients fulfill any of the previous criteria for which treatment would be instituted.

Those few who treat more vigorously quote the V.A. studies⁴ showing a tendency to reduction in morbidity from thromboembolism, and their own

ANTICOAGULATION AND ACUTE MYOCARDIAL INFARCTION

BACOS

view that the morbidity from acute anticoagulation in their hands is negligible.

All agree that the incidence of clinically apparent emboli is far less than 10%, and more in the region of 5% with only a rare death being attributed to massive systemic or pulmonary embolus. This agrees with the author's own experience, though stated reports have indicated that deaths from embolism may be as high as 10-20%.⁵ Either this again is an inaccurate estimate on the part of area cardiologists or the low frequency suggests that we are intuitively defining those "poor risk" patients and treating them accordingly. Russek⁶ in 1953 divided patients into good and poor risks defining those with a propensity for emboli as patients with one or more of the following: A large infarct, shock, serious arrhythmia, cardiac enlargement, previous infarction or complicating diseases. Area cardiologists would appear to agree with some but not all of these criteria.

Short-term inhouse anticoagulation, until ambulation is actively attained, is the approach used by 23 cardiologists while the eight who continue anticoagulants beyond hospitalization vary from two weeks to six months to one year and one physician employs them indefinitely. The question of when to stop anticoagulants has always been a polemic issue and there are at least two good studies^{1,7} to suggest that anticoagulation on a long-term basis actually does reduce mortality, especially in those patients with prolonged angina or previous infarction. This would appear to be paradoxical in view of studies showing no difference in mortality with anticoagulants in the acute period. A recent issue of Medical Letter⁸ refers to these studies and compounds the confusion by concluding that the difference in mortality is not significant. Most of the area cardiologists are so impressed with the significant morbidity and mortality due to long-term anticoagulants that they clearly eschew this approach.

To sum up, the criteria for the employment of anticoagulant therapy in acute myocardial infarction are not clearly defined. There is no doubt that intravascular clotting does attend acute myocardial infarction and the literature clearly supports the efficacy of anticoagulation in preventing thromboembolism. Area cardiologists would agree with this but it would appear that there is a great deal of individualization. Moreover, their individual responses would indicate a wide variation of interpretation of available data and perhaps prejudice based on their own experiences. Generally, it can be said that the patient with profound or repeated

infarction, with congestive failure and/or complications requiring prolonged inactivity appears to be a suitable candidate for anticoagulation.⁸

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Department of Cardiology
Washington Hospital Center

References

1. Report of the Working Party on Anticoagulant Therapy In Coronary Thrombosis to the Medical Research Council: Assessment of short-term anticoagulant administration after cardiac infarction, *Brit. Med. J.*, 1969, 1:335.
2. WRIGHT, O.S., MARPLE, C. C., BECK, D. F.: Myocardial Infarction, Its Clinical Manifestations and Treatment with Anticoagulants, A Study of 1,031 Cases. New York, Grune & Stratton, Inc. 1954.
3. Handley, A. J. et. al: *Br. Med. J.*, 1972, 2:436.
4. Veterans Administration Cooperative Clinical Trial, *JAMA*, 1973, 225:724.
5. Ebert, R. V.: Use of Anticoagulants in Acute Myocardial Infarction. *Circulation*, 1972, 903.
6. Russek, H. I. Therapeutic considerations and controversial issues in the modern management of myocardial infarction, *Amer. J. Med. Sci.*, 1953, 225:589.
7. Hilden, T., Iversen, K., Raaschou, F., Schwartz, M.: Anticoagulants in acute myocardial infarction, *Lancet*, 1961, 2:327.
8. The Medical Letter on Drugs and Therapeutics, 1974, 16:17.

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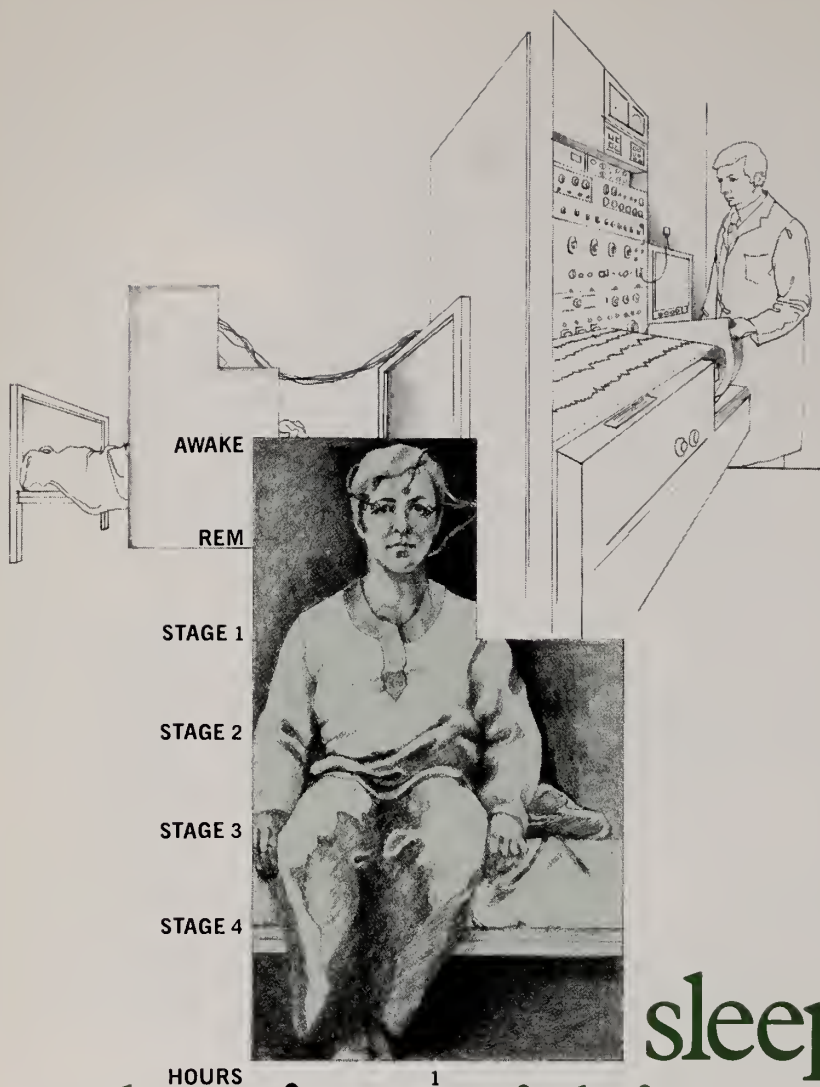
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Precautions: In elderly and debilitated, initial dosage should be limited to 15 mg to preclude oversedation, dizziness and/or ataxia. If combined with other drugs having hypnotic or CNS-depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with latent depression or suicidal tendencies. Periodic blood counts and liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported were headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins and alkaline phosphatase. Paradoxical reactions, e.g., excitement, stimulation and hyperactivity, have also been reported in rare instances.

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REFERENCES: 1. Kales A, et al: *Arch Gen Psychiatry* 23:226-232, Sep 1970

2. Karacan I, Williams RL, Smith JR: The sleep laboratory in the investigation of sleep and sleep disturbances. Scientific exhibit at the 124th annual meeting of the American Psychiatric Association, Washington DC, May 3-7, 1971

3. Frost JD Jr: Data on file, Medical Department, Hoffmann-La Roche Inc, Nutley NJ

4. Vogel GW: Data on file, Medical Department, Hoffmann-La Roche Inc, Nutley NJ

5. Dement WC: Data on file, Medical Department, Hoffmann-La Roche Inc, Nutley NJ

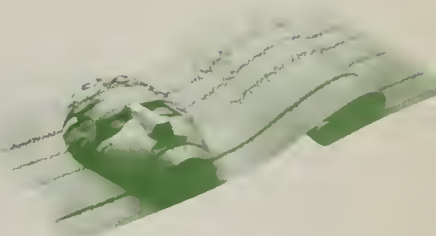
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Is there a need for a drug compendium?

A drug compendium of the type I envision would fill a definite need for the practicing physician. Such a compendium would give him all the information necessary for using

a drug intelligently, and it would do so in a clear, concise, convenient, objective and balanced fashion.

What a Compendium Should Contain

I believe the compendium should inform the doctor what a drug will do, when he should use for what type of patient, for how long, in what dose, what benefits his patient is likely to obtain, the risks involved, and cross-reaction with other drugs.

The information would be based on the package insert and have the same legal status. In fact a complete compendium with complete and current information might even eliminate the necessity

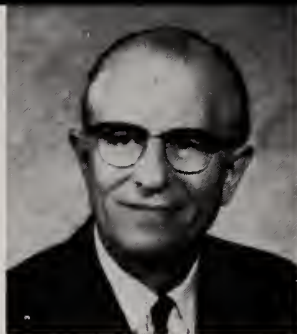
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A drug compendium, or preferably compendia, should, I believe, be private, not federal, in sponsorship. They should contain comprehensive listings of drugs available for prescribing. They should be single, legibly printed volumes of reasonable size, updated quarterly or semiannually and completely revised every year.

Function of a Compendium

A compendium should furnish the following information on drugs in the following order: indications for use, side effects, adverse drug reactions, contraindications, drug interactions, drug dosage at the dosage forms marketed. Drug prices should not be included because they vary so widely and change rapidly.

No compendium should set forth drugs of choice or discuss relative efficacy. Such questions must be left for the practicing physician to decide, whether on the basis of the medical literature, his own clinical experience, advice of colleagues, information supplied by manufacturers, and so on.

Nor should a compendium undertake to educate the doctor how to use drugs. Rather, it must be a reference source designed primarily to refresh his memory as to drugs he may not use regularly. I

for a package insert in many instances. This would constitute a substantial saving for the manufacturer.

By a complete compendium, I do not mean a volume of prohibitive size. You don't need a book describing 25,000 products with an enormous amount of repetition. Rather, drugs should be arranged by class. Mutually applicable information would be provided, along with brief discussions pinpointing differences in specific drugs of that class. Listings would be cross-indexed in a useful way.

Other Available Documents as Sources of Information

Existing references such as PDR and the AMA Drug Evaluation are obviously useful but they are incomplete. Either they are not cross-referenced by generic name and do not group drugs with similar characteristics, or they do not list all the available and legally marketed drugs. And some of those omitted may be very useful.

should in no way imply control over the practitioner's prerogatives.

Why Another Compendium?

A practicable, single-volume compendium cannot, nor is it necessary to, include all drugs on the market today. From my practice of internal medicine for some 15 years, my experience as a consultant, and as a faculty member of four or five medical schools, I would estimate that a doctor uses only 30 to 35 drugs regularly. The 1972 Physicians' Desk Reference, incidentally, contained about 2,500 entries.

As to whether there should be a federal compendium, in my opinion, as stated earlier, the answer is easy—there should *not* be one. The proposal assumes that existing compendia are inadequate. We're not sure of that at all. Whatever its imperfections, the present drug information system in the U.S. is open, multifaceted, pluralistic and extensive. Good compendia exist, as well as other ample sources on drug therapy, ranging from journal literature through AMA Drug Evaluation to company materials. Not all physicians may use such sources as often or as well as they should, but that is the fault of the man, not of the sources.

In any event, rather than pro-

On the other hand, drugs made by more than one supplier, tetracycline for example, may be fully described a dozen times in the same book.

While perhaps PDR could be rearranged and cross-indexed with generics included, and while the AMA Drug Evaluation might also be modified and expanded, I am not sure that the end result would have all the attributes required for a useful compendium. At the same time, you would run the risk of amassing a voluminous and unwieldy tome.

Should Editorial Comments Accompany the Listings?

Subjective judgments, in my opinion, have no place in a compendium. However, if there is substantial evidence based on a sound body of science concerning relative efficacy of several drugs, certainly that information should be included. The committee of experts compiling and editing a particular section would also have to assess

duce another book, it makes much more sense to work on improving existing compendia, and perhaps they could, as knowledge advances, include more accumulated clinical data and experience, and more information on drug interactions and adverse reactions.

Implications of a Federal Compendium

Take a hard look at the implications of a federal compendium. It would have the force of law, virtually dictating what drugs to use and how to use them. In effect, it would be a regulatory document with legal or quasi-legal status, posing medical/legal problems similar to those the doctor may now encounter if and when he departs from the provisions of the package insert. A compendium under federal aegis would tend to restrict decisions on drug therapy to one orthodox level—a most dangerous trend for medicine.

New Compendium—A Medical Option

I detect no ground swell of initiative or support whatsoever for a federal compendium—or, for that matter, for a new compendium of any type. A 1969 PMA survey conducted by Opinion Research Corporation found that only 15 per

and indicate instances where a meaningful difference between drugs is pertinent.

Sponsorship, Compilation and Editing

Producing a book like this would undoubtedly be difficult and demanding. It would obviously take a great deal of talent and expertise, and would require a varied and experienced group, ranging from writers and editors to highly skilled clinicians and pharmacologists. Style, format and clarity of language would play an important part in determining the usefulness of the book. And it should be updated periodically and completely revised annually.

I have no opinion whether the government or the private sector should sponsor and/or finance the compendium. What is most important is that the compendium be an authoritative, objective and useful source of information for the doctor to have at hand as a ready reference.

cent of those physicians interviewed felt a new compendium was needed. And a large majority did not favor the involvement of the federal government if one were to be created, preferring instead a nongovernmental consortium.

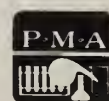
Even if we come to a time when the medical profession itself opts for a new kind of compendium, it should be handled and financed, ideally, outside both government and industry. Final review and editorial authority could be delegated, say, to specialty bodies and medical societies—but above all, *not* the government.

Surely the health care system in the United States has far more vital matters to consider than the extensive cost and effort that would have to go into the preparation and maintenance of a new, monolithic compendium, and especially one bearing the imprimatur of the federal government.

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SCIENTIFIC ARTICLES

Peripheral Coronary Artery Perfusion for Direct Coronary Artery Reconstruction

LAWRENCE J. FREANT, M.D., LUIS A. MISPIRETA, M.D. and KAREL B. ABSOLON, M.D.

Abstract

The incidence of enzymatic or ECD changes due to coronary bypass is cited as being from 9% to 44%. This led to the development of the technique of catheter peripheral coronary artery perfusion reported here. The technique permits direct surgical reconstruction, and is promising in regard to the development of fewer post-perfusion abnormalities attributable to ischemia. The indications for direct perfusion are discussed, as are the causes of myocardial infarction following coronary surgery.

Introduction

The incidence of acute myocardial infarction or ischemic injury ranges from 9% to 44% in coronary bypass surgery.¹⁻³ This disturbing complication has been in the past ascribed to technical mishap or immediate closure of the bypass graft.¹⁻³ The definition of myocardial infarction varies from electrocardiographic findings of acute infarction⁴⁻⁵ to cardiac enzyme elevations⁴ and a clear cut depression of left ventricular function during the use of continuous hemodynamic monitoring. The surgeon must accept the responsibility for such changes, even though patency of grafts in presumably infarcted areas is demonstrated and patients have been completely rehabilitated with loss of all

... all patients have been managed with high flow total cardiac bypass, fibrillatory arrest, left ventricular decompression and moderate hypothermia. Aortic crossclamping has been avoided and air emboli during arterial reconstruction have been prevented...

anginal symptoms and with an improved exercise tolerance.⁴ The technical aspects of constructing coronary artery bypass grafts are presently well standardized.⁶⁻¹¹

Causes of Acute Myocardial Infarction After Direct Coronary Artery Revascularization.

The various causes may be:

1. Anoxia within a segment of myocardium supplied by a partially obstructed coronary artery which is totally occluded during reconstruction.
2. Inadequate collateral circulation to a partially obstructed main coronary artery branch to which a graft is applied.
3. Air emboli and thrombi.

4. Technical mishaps in performing the anastomoses; such as development of dissecting intimal flaps obstructing sutures about the critical distal portion of the anastomoses or kinking.
5. Disproportionate sizes of the grafts with respect to the vessel to be bypassed with turbulence of flow predisposing to thrombosis.

An additional contributing factor may be ischemic cardiac arrest while crossclamping the ascending aorta to provide a dry operating field. Hypoperfusion on the heart-lung machine may have an effect on a myocardium supplied by severely obstructed coronary vessels.

Material and Methods

In order to minimize these hazards a direct perfusion technique has been developed at the Washington Hospital Center. (Figure 1) A polyethylene catheter has been adapted. The two catheters currently in use measure .027 cm. and .034 cm. in internal diameter. The outside diameters of the catheters measure .046 cm. and .063 cm. respectively. Because of the pliability of the catheters it has been possible by gently drawing their tips to perfuse coronary vessels of less than 2 mm. in internal diameter. The catheter is connected to a one-eighth inch silastic coronary perfusion tubing

CORONARY PERFUSION FOR CORONARY RECONSTRUCTION

FREANT, MISPIRETA AND ABSOLON

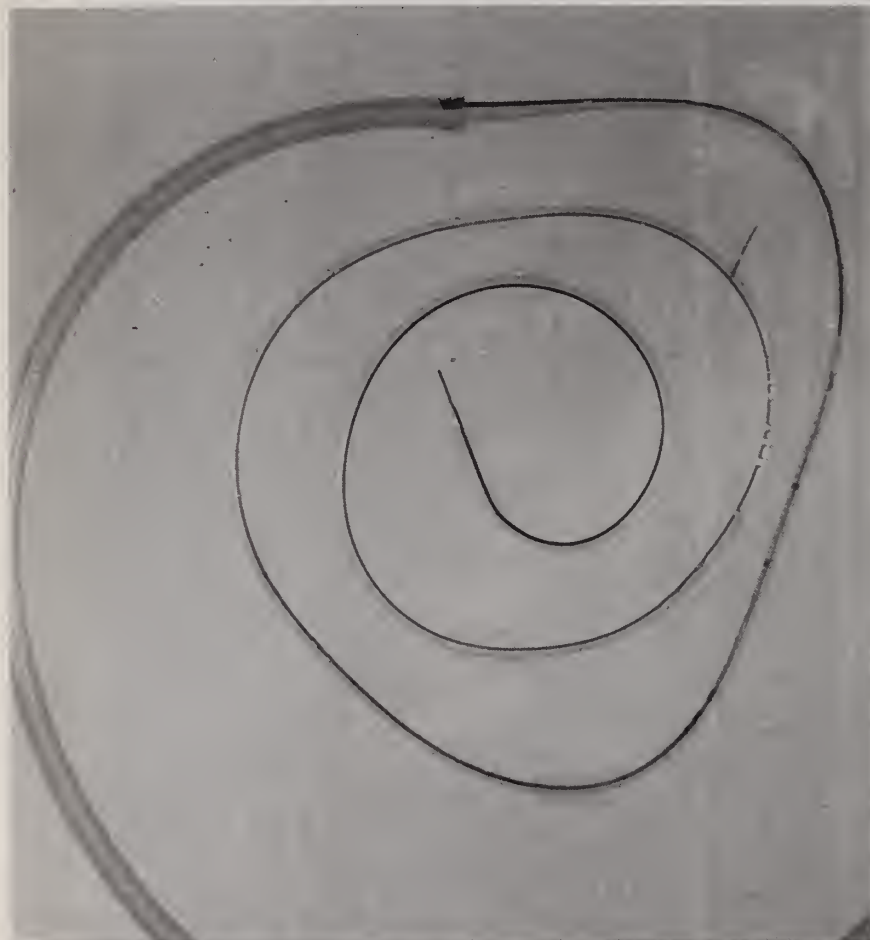


FIG. 1. Coronary Perfusion Catheter.

(diameter 1/8"), which is attached to the coronary reservoir and placed through the coronary perfusion pump head. There is a linear relationship of the catheter flows to the revolutions per minute of the coronary pump head up to flows of 104 ml/min. (Figure 2)

Clinical Application

Upon incising the coronary artery longitudinally the catheter is inserted

peripherally. When forward flow is established the vessel is gently occluded proximally by compression. Flows of 20 to 60 ml/min at pressures of 70 to 100 mm Hg. have been used through branches of the right and left coronary arteries. Care is taken to avoid introduction of air in the distal tree with insertion of the catheter and the gentle placement of the catheter through the arteriotomy avoids injury. The anastomoses, using the internal

mammary artery for most left sided lesions and the saphenous vein for most of the right, is begun with interrupted 7-0 Tevdek or Prolene sutures about the critical distal one-third of the arteriotomy. The placement of these sutures is facilitated by gentle distension of the blood vessel with the catheter. Furthermore, elimination of troublesome back bleeding through the collaterals can be accomplished for more accurate suture placement without cross clamping of the ascending aorta. The side of the anastomosis is completed with running or interrupted everting sutures and the perfusion catheter is removed before the final interrupted proximal sutures are inserted. In this manner time intervals with no coronary perfusion were less than three minutes.

Discussion

At present eight patients have undergone coronary artery bypass using this technique at the Washington Hospital Center. In addition to peripheral coronary perfusion, all patients have been managed with high flow total cardiac bypass, fibrillatory arrest, left ventricular decompression, and moderate hypothermia. Aortic crossclamping has been avoided and air emboli during arterial reconstruction have been prevented with the use of the perfusion cannula.

The use of the perfusion cannula stint during the period of the anastomosis has been of definite technical advantage for reconstruction of minute coronary vessels. In experiments on dogs peripheral coronary perfusion prevented development of myocardial infarction of the anterior descending coronary artery which invariably developed upon ten minutes cross-clamping.

Current indications for the use of direct coronary perfusion during coro-

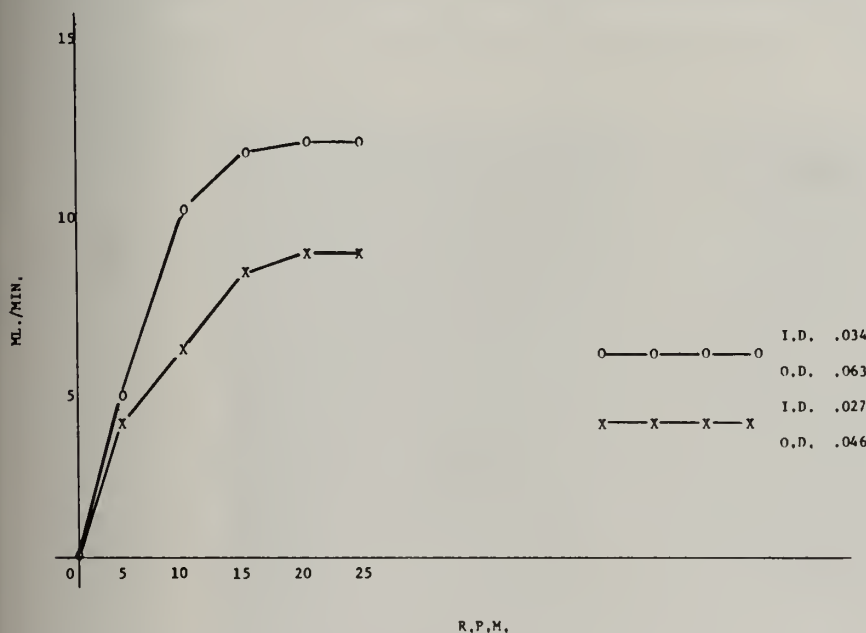


FIG. 2. Coronary Perfusion Cannulae Flow.

nary revascularization at the Washington Hospital Center include-

1. Acute proximal obstruction in the left main coronary artery or in the left anterior descending coronary proximal to the first septal perforator.
2. Proximal obstruction of 75% of coronary vessel without demonstrated collaterals distal to the block.
3. All short proximal obstructions of 75% with or without demonstrated collaterals.
4. Collateral circulation filling either branches of the right or left coronary system in a retrograde fashion when bypass to the dominant coronary artery supplying the forward flow is performed.
5. When bypass to more than one coronary is planned.

References

1. FAVALORO, R., EFFLER, D., GROVES, L., SONES, F., FERGUSON, D.: Myocardial revascularization by internal mammary artery implant procedures: clinical experience. *J. Thorac. Cardiovasc. Surg.*, 1967, 54:359.
2. HULTGREN, H., MIYAGAWA, M., BUCK, W., ANGELL, W.: Ischemic myocardial injury during coronary artery surgery. *Am. Heart J.*, 1971, 82:624.
3. DIETRICH, E., LIDDICOAT, J., FLESSI, F., KINARD, S., DEBAKEY, M.: Serum enzyme and electrographic changes immediately following myocardial revascularization. *Ann. Thorac. Surg.*, 1968, 5:195.
4. BALOOKI, H., SOMMER, L., FORALDO, A., GHABRAMAIW, A., SLAVIN, D., KAISER, C.: The significance of serum enzyme studies in patients undergoing direct coronary artery surgery. *J. Thorac. Cardiovasc. Surg.*, 1973, 65:863.

5. BENCHIMAL, A., PROMISLOFF, S., DESSER, K.: Electrovectorcardiographic changes after proximal right coronary artery venous bypass and distal endarterectomy. *Am. J. Cardiol.*, 1972, 30:466.
6. ABSOLON, K. B., AUST, J. B., LILLEHEI, C. W.: Coronary endarterectomy and graft replacement. *A.C.S. Clinical Congress News*, 1955, p 9.
7. ABSOLON, K. B., AUST, J. B., VARCO, L. R., LILLEHEI, C. W.: Surgical treatment of occlusive coronary artery disease by endarterectomy or anastomotic replacement. *Surg. Gynecol. Obstet.*, 1956, 103:180.
8. ABSOLON, K. B., LEWIS, E. H., BASHOUR, F.: Simultaneous peripheral coronary endarterectomy and bypass graft. *Surg. Gynecol. Obstet.*, 1971, 132:1083.
9. ABSOLON, K. B.: Magnification for direct coronary artery surgery. *Bull. of Med. Stf. of Methodist Hosp. of Dallas*, 1971, 4:214.
10. ABSOLON, K. B., MISPIRETA, L. A., SEREMETIS, W., KESHISHIAN, J.: Simultaneous anterior ventricular aneurysm repair, coronary endarterectomy, coronary bypass graft and abdominal aortic graft replacement. *Bull. de la Societe Internationale de Chirurgie*, 1973, p 1.
11. ABSOLON, K. B., MISPIRETA, L. A.: The past, present and future of the surgical treatment of atherosclerotic heart disease. Review of Surgery-in Press.
12. ABSOLON, K. B.: Unpublished data.

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THE VIEW BOX

Prepared by The Department of Radiology Washington Hospital Center

A young female consults her physician because of a cough, productive of brownish material. This is present for several weeks and she has no other symptoms except for retrosternal pain.

(for diagnosis see page 262)



Carotid Artery Replacement with a Saphenous Vein Graft for Other Than Arteriosclerotic Obstructive Disease

KRISTIN STUEBER, M.D., ARNALDO A. GARRO, M.D. AND KAREL B. ABSOLON, M.D.

Abstract

Two patients with other than arteriosclerotic obstruction of the carotid artery are reported, one as part of a laryngectomy with extensive tumor and the second with total traumatic obstruction. In young patients with traumatic occlusion of the carotid artery, especially if future trauma is expected, direct repair or a saphenous vein graft is the procedure of choice. In carotid artery replacement for tumor involvement, saphenous vein graft replacement is the procedure of choice, especially if ionizing radiation is planned postoperatively.

Introduction

Reconstruction of the cerebral circulation and especially of the common carotid artery and its bifurcation has become a common procedure for the relief of cerebral ischemia of arteriosclerotic origin. The following report concerns carotid artery replacement for carotid artery involvement other than arteriosclerosis.

Since the report by Eastcott, Pickering and Rob⁴ there have been many reports^{3,7} on the use of endarterectomy, with or without venous or synthetic patch grafts, and the use of synthetic bypass grafts as methods of providing this reconstruction of the

vessel. DeBakey³ presented an extensive report on the use of bypass procedures with synthetic materials while Pierangeli *et al.*⁷ presented the use of autologous vein grafts. Dale and Mavor² showed that autogenous vein grafts had a better patency rate and longevity in small vessels than synthetic material.

This report concerns carotid artery replacement for carotid artery involvement other than arteriosclerosis.

In the following two cases of carotid artery replacement by autogenous saphenous vein, the first patient had a carotid resection as part of a laryngectomy for an extensive tumor invading the carotid artery. The second is an example of total traumatic obstruction of the common carotid artery, in a young patient, successfully replaced with autogenous saphenous vein.

The reason for the use of autogenous vein in the first patient was the necessity of using ionizing radiation postoperatively; in the second patient, an athlete, a saphenous vein was felt to be more resilient to possible future trauma.

Case Presentation

The first patient, a 63-year-old male, presented with hoarseness of about eight months duration. Physical examination on admission showed a large primary lesion in the left pyriform sinus and a large metastatic lesion in the left upper jugular group of lymph nodes. A biopsy on August 11, 1972 showed the primary tumor to be an epidermoid carcinoma of the larynx.

Operation: The patient had a laryngectomy and left radical neck dissection performed in the usual manner. As the dissection of the jugular vein was carried cephalad an obstruction of the vein by the metastatic tumor mass was noted. It was also found that the mass was invading the left common carotid artery. The dissection was then started at the mastoid process and carried caudal. Once the area of adherence of the tumor to the common carotid was isolated, resection of the common carotid artery was carried out *en bloc*. The proximal to distal carotid artery shunt maintained cerebral circulation and the greater saphenous vein was interposed with an end-to-end anastomosis using 6-0 Tevdek everting continuous suture technique. The postoperative course was uneventful. The patient received 3000 Rads of ionizing radiation. A subsequent angiogram showed a patent graft. (Figure 1)

CAROTID REPLACEMENT WITH SAPHENOUS FOR NON-ARTERIOSCLEROTIC DISEASE

STUEBER, GARRO AND ABSOLON



FIG. 1. Patient No. 1. Postoperative arteriogram of a saphenous vein graft replacing the left common carotid artery resected for invasion by squamous cancer of larynx.

Subsequently the patient developed metastatic disease in the right neck and had a radical neck dissection performed on that side.

Involvement of the carotid artery must be considered a sign of incurability. Carotid artery replacement should be therefore performed only in exceptional cases.

The second patient was a 17-year-old male high school student who sustained blunt trauma to the anterior chest and right anterior neck during football practice. Immediately afterwards he noted blurred vision, white spots in his vision and frontal headaches. These symptoms cleared spontaneously and without sequelae. He noted no weakness and paresthesias in any extremity. About one week later he had an episode of blindness in the right eye, lasting a few hours.

Initially physical, ophthalmological and neurological examinations were within normal limits. The absence of pulse of the right common carotid artery was explained by an arteriogram which showed occlusion of the right common carotid artery at its origin.

Operation: The right innominate and carotid arteries were exposed through a cervical incision with extension to the upper mediastinum by division of the sternum to the second intercostal space. The carotid artery was found to be occluded from its origin at the innominate artery to the bifurcation. The occluded segment was resected and a segment of the greater saphenous vein was interposed end-to-end between the innominate and internal carotid arteries using 6-0 Tevdek and an everting continuous future technique. Follow-up showed graft patency. (Figures 2, 3, 4) This patient was seen eighteen months later and had a good pulse above the insertion of the vein graft. He was also actively engaged in collegiate football.



FIG. 2. Patient No. 2. Preoperative arteriogram showing complete traumatic occlusion of the right common carotid in a 17-year-old football player; the vertebral artery is patent.

Discussion

In 1953 Conley¹ described the use of autogenous vein grafts as emergency replacement for ruptured common carotid arteries after irradiation. Six patients in whom carotid arteries were replaced with saphenous vein grafts healed without complication. All were patent up to eight months postoperatively when the patients died from either recurrent tumor or other causes.

Trauma to the carotid artery with subsequent thrombosis was evaluated by Gurdjian *et al.*⁵ Of the three cases of carotid injury two had immediate onset of symptoms and one had onset two weeks later. The two patients with immediate symptoms had stenosis at the bifurcation on arteriography. One had no operative procedure performed and recovered some function, while the second had an endarterectomy with subsequent occlusion. The third patient on arteriography showed occlusion of the left internal carotid artery and at exploration an intimal tear was repaired. Postoperative arteriogram showed a narrowed but patent vessel. In another report⁹ stenosis at the site of carotid injury developed and endarterectomy was the treatment of choice.

It is the authors' impression that for a young patient, especially an athlete who expects to resume his previous activity, a pliable autologous saphenous vein is the prosthetic material of choice for carotid artery replacement. Autologous materials are more likely to withstand direct or indirect trauma, especially if small vessels are replaced. It is likely that a saphenous vein graft is more likely to withstand ionizing radiation and its inflammatory sequelae than is a synthetic graft.

CAROTID REPLACEMENT WITH SAPHENOUS FOR NON-ARTERIOSCLEROTIC DISEASE

STUEBER, GARRO AND ABSOLON

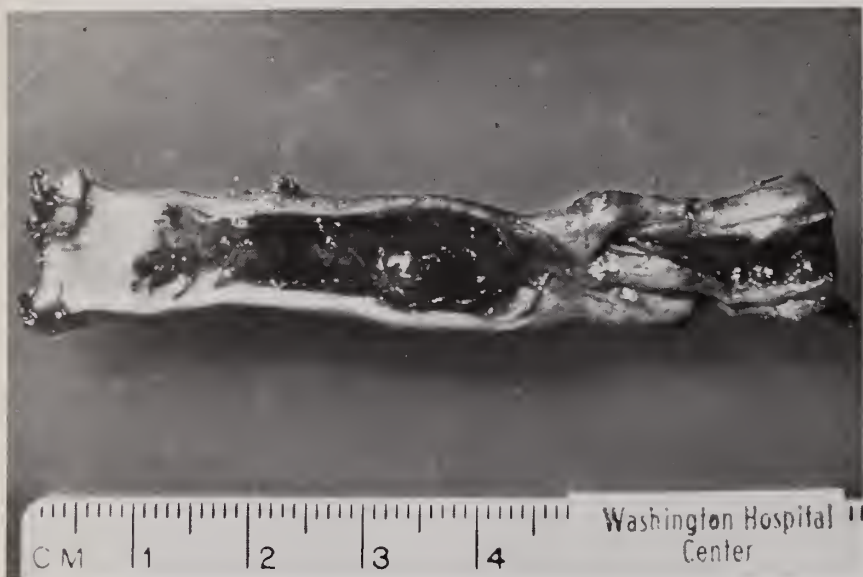


FIG. 3. Patient No. 2. The operative specimen of occluded right carotid artery.



FIG. 4. Patient No. 2. Postoperative arteriogram in place of the right common and proximal internal carotid arteries.

References

1. CONLEY, J. J.: Free autogenous vein graft to the internal and common carotid arteries in the treatment of tumors of the neck. *Ann. Surg.*, 1953, 137:205.
2. DALE, W. A., MAVOR, G. E.: Peripheral vascular grafts. Experimental comparison of autogenous veins, homologous arteries and synthetic tubes. *Brit. J. Surg.*, 1959, 46:305.
3. DEBAKEY, M. E.: Surgical considerations of the innominate, carotid, subclavian and vertebral arteries. *Ann. Surg.*, 1961, 154:698.
4. EASTCOTT, H. G., PICKERING, G. W., ROB, C. G.: Reconstruction of internal carotid artery in patient with intermittent attacks of hemiplegia. *Lancet*, 1954, 2:994.
5. GURDJIAN, E. S., *et al.*: Closed cervical cranial tumor associated with involvement of carotid and vertebral arteries. *J. Neurosurg.*, 1963, 20:418.
6. MOORE, O. S., KARLAN, M., SIGLER, L.: Factors influencing the safety of carotid ligation. *Am. J. Surg.*, 1969, 118:666.
7. PIERANGELI, A., *et al.*: Use of saphenous vein in reconstructive surgery of peripheral arteries. *Minerva Cardioangiol.*, 1969, 17:1007.
8. SPARKS, C. H., MELGARD, M. A., ROAF, J.: Carotid artery replacement with reinforced autogenous vein grafts. *Angiology*, 1963, 14:542.
9. TOAKLEY, G., MCCAFFREY, J.: Traumatic thrombosis of the internal carotid artery. *Aust. New Zeal. J. Surg.*, 1965, 34:261.

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Five Year Followup of Colonic Transplants in Patients with Epidermolysis Bullosa Producing Esophageal Obstruction

RANDOLFO DE LEON, M.D., LUIS A. MISPIRETA, M.D. AND KAREL B. ABSOLON, M.D.

Abstract

This report concerns four patients suffering from the dysplastic form of epidermolysis bullosa congenita treated by surgical reconstruction. It is concluded that total replacement of the thoracic esophagus is the treatment of choice and offers complete rehabilitation of such patients, as the five year follow-up indicates.

Introduction

This account summarizes basic information on epidermolysis bullosa in forty patients, especially with respect to esophageal lesions.¹⁻¹⁷ The esophagus seems to be affected primarily by the dystrophic form of epidermolysis bullosa. Persistence in performing repeated esophagoscopies and dilatations may cause more damage than benefit. Gastrostomy helps these patients but does not prevent regurgitation and/or aspiration of their own secretions.⁷ A retrosternal colonic conduit from the cervical esophagus to the stomach seems to be a logical operation to relieve the block.

Two patients suffering of the dysplastic type of epidermolysis bullosa with associated esophageal strictures were treated with a colonic bypass graft. The one to two year follow-up was reported previ-

ously.^{1,2-14} The present report concerns the five year follow-up of the two patients, evidencing that they have obtained relief of their symptoms and are able to live a basically normal existence.

The clinical picture, the various types, diagnosis and natural history of this entity have been discussed in the literature.^{1,2} The etiology is unknown, and there is no specific treatment. Antibiotics are essential for combating infections in these bullae, which have no specific histological or histochemical features.³ The diagnosis is based on history and clinical findings. The dysplastic type of epidermolysis bullosa is disabling. Repeated ulcerations lead to scar contractures of the flexor surfaces of the extremities and epithelial webbing and pseudosyndactylism of the hands and feet.^{4,5} The skin is very thin and appears shiny and parchment-like. The nails are frequently deformed or absent. Involvement of the esophageal mucosa with stricture may occur.^{6,7}

Nix and Christianson⁸, Bergenholtz⁹, Wey and Schnyder⁷ described patients with involvement of the esophagus. It is generally agreed that trauma is the initiating cause of the esophageal process, ending in fixed stenosis with dysphagia.¹⁰ Endoscopic examination and repetitive bougienage under anesthesia used to be the recom-

mended treatment. Temporary relief was provided, but it unfortunately traumatized the esophageal mucosa causing submucosal bullae, detaching the mucosa from underlying tissues, and producing even more stricture formation (plus instrumental or spon-

The esophagus seems to be affected primarily by the dystrophic form of epidermolysis bullosa . . . retrosternal colonic conduit from the cervical esophagus to the stomach seems to be a logical operation to relieve the block.

taneous perforation).⁶ Catastrophies of this kind were reported as the terminal events of the disease.¹¹

Esophageal Replacement in Epidermolysis Bullosa

The barrier to the replacement of the esophagus in this disease was largely psychologic. It was due to a lack of information and perhaps lack of regard for patients suffering from a condition of unknown etiology for which no specific treatment was

FOLLOWUP OF COLONIC TRANSPLANTS IN EPIDERMOLYSIS BULLOSA

DE LEON, MISPIRETA AND ABSOLON

known.^{1,2} As previously reported in detail,^{13,14} bypass from the esophagus to the stomach with a retroperistaltic right and transverse colon in two boys, eight and 12 years, was performed, placing the conduit retrosternally and posterior to the stomach. The results of this surgical technique of esophageal replacement in such patients in the early follow-up was gratifying, but the question arose of whether the results would be permanent. This report is based on evaluation five years after the original procedure, (Figures 1 and 2), which demonstrated satisfactory function and growth of the colonic interposition graft in the two boys affected with this disabling disease.

At the present both patients are asymptomatic. They are able to tolerate a regular diet. The first patient (Case #1) measures 70" and weighs 105 lbs. which as to height corresponds to the 90 percentile and as to weight to the 75 percentile. The second patient (Case #2) measures 73" and weighs 122 lbs., which as to height corresponds to the 97 percentile, weight to the 25 percentile.

Case Reports

Case No. 1: A white male 8-year-old was hospitalized with history of progressive dysphagia of five year's duration with typical lesions of epidermolysis bullosa on his hands, feet and mouth. An esophagogram demonstrated a stricture 4 cm. long above the carina. On esophagoscopy the site of stricture could not be passed. On May 15, 1968 retrosternal colonic transplant, pyloroplasty, and Stamm gastrostomy were accomplished.

Care No. 2: A white male 12-year-old was hospitalized with the same diagnosis and progressive dysphagia. Esophagograms showed diffuse stricture of the thoracic esophagus. In view of the complete rehabilitation of



FIG. 1. Five year follow-up of colonic transplants in pts. with epidermolysis bullosa producing esophageal obstruction.

FIGS. 1 and 2. Showing barium swallow demonstrating patency of colonic bypasses—five years after original surgery in two patients.



FIG. 2. Five year follow-up of colonic transplants in pts. with epidermolysis bullosa producing esophageal obstruction.

the swallowing function of his younger brother, the patient clamored for relief. On July 16, 1968 he underwent a retrosternal colonic transplant using the same procedure as in the first case.

The postoperative course was uneventful with the exception of the characteristic skin changes in the operated areas. The patients resumed a regular diet one week postoperatively. Followup esophagograms demonstrated satisfactory function of the colonic conduits and with, especially, no stricturing at the anastomotic site.

Follow-up:

Both patients did well, remained on a regular diet, gained weight and grew up to normal size. In 1971, three years after the original surgical procedure, the older of the patients (Case #2) at the time of removal of the residual thoracic esophagus through the right chest developed a leak from the esophagocolonic anastomosis. A right-sided empyema resulted which necessitated drainage and a second to fourth rib thoracoplasty. Resection of the residual intrathoracic esophagus was performed prophylactically because some 15% of patients with this disease were found to develop cancers of the squamous epithelium at an early age.^{15,16} The residual esophagus showed no evidence of neoplasia. All that remained was a string-like band with the lumen remaining patent only in isolated segments.

On June 22, 1972 the cervical fistula of the colonic transplant was excised and a hypopharyngeal esophagus to colonic graft anastomosis accomplished. The postoperative course with the exception of pulmonary atelectasis was uneventful. Ten days after surgery barium swallow showed good function of the repair, and subsequent course was uneventful.

FOLLOWUP OF COLONIC TRANSPLANTS IN EPIDERMOLYSIS BULLOSA

DE LEON, MISPIRETA AND ABSOLON

Comment

The involvement of the esophagus in epidermolysis bullosa dystrophica with its sequela of stricturing and aspiration pneumonia has been substantiated widely in the literature.^{11,17} The senior author^{13,14} had reviewed the literature and described two new cases which were treated for the first time with reconstruction, that is, a retrosternal colonic conduit, in 1968. It is concluded that this method is the most adequate form of treatment. It relieves these patients of their dysphagia, prevents aspiration, and offers an essentially normal existence.

Since 1968 one more patient underwent total thoracic substitution with a colon graft and an equally gratifying result.¹⁸ Another patient suffering from the dysplastic form of epidermolysis bullosa and a localized cervical esophageal stricture was successfully treated by excision of the mucosal stricture.¹⁹

References

- GEDDE-DAHL, T. JR.: Epidermolysis bullosa: A clinical, genetic and epidemiological study. The Norwegian Research Council for Science and The Humanities. 1971. Published in U.S.A. by Johns Hopkins Press, Baltimore, Maryland.
- GORLIN, R. J.: Epidermolysis bullosa. *Oral Surgery*, 1971, 32:760.
- HADIRY, M., MCDONALD, A. F.: Epidermolysis bullosa. *Br. J. Radiol.*, 1960, 33:646.
- PERS., M.: Skin grafting in a case of epidermolysis bullosa. *Acta Chir. Scand.*, 1965, 129:333.
- REES, T., SWINYARD, C. A.: Rehabilitative digital surgery in epidermolysis bullosa. *Plast. Reconstr. Surg.*, 1967, 40:169.
- STOUT, P. S.: Recurring stricture of the esophagus due to epidermolysis corrosa. *Laryngoscope*, 1929, 39:470.
- WAY, W., SCHNYDER, V. W.: On the treatment of esophageal stenosis associated with epidermolysis bullosa hereditaria. *Dermatologica* (Basel), 1964, 128:173.
- NIX, T. E. JR., CHRISTIANSON, H. B.: Epidermolysis bullosa of the esophagus: Report of two cases and review of the literature. *South. Med. J.*, 1965, 58:612.
- BERGENHOLTZ, A., OLSON, O., ARNILL, T., LUNSTROMM, N. R.: Epidermolysis bullosa hereditaria dystrophica. *Arch. Klin. Exp. Dermatol.*, 1963, 217:518.
- KATZ, J., GRYBOSKI, J., ROSENBAUM, H. M., SPIRO, H. M.: Dysphagia in children with epidermolysis bullosa. *Gastroenterology*, 1967, 52:359.
- SADLER, R. L.: Dysphagia pneumonitis following epidermolysis bullosa. *Br. J. Tuberc.*, 1955, 49:142.
- ABSOLON, K. B.: Surgical considerations of epidermolysis bullosa. *Bull. de la Soc. Internationale de Chirurgie*, 1970, 3.
- ABSOLON, K. B., FINNEY, L. A., WADDIL, G. M., HATCHETT, G.: Esophageal reconstruction—colon transplant—in two brothers with epidermolysis bullosa. *Surgery*, 1969, 65:832.
- ABSOLON, K. B., MOORE, J. R., KOLLMAR, G. H., WADDIL, G. M., HUTCHINSON, V. A.: Esophageal colonic grafts in two siblings with epidermolysis bullosa. *Bull. of Med. Stf. of Methodist Hospital of Dallas*, 1970, 4:36.
- GORLIN, R. J., CHANDHRY, A. P.: Unusual stomadromes. *Oral Surgery*, 1960, 13:262.
- WECHSLER, H. L., et al.: Polydysplastic epidermolysis bullosa and development of epidermal neoplasms. *Arch. Dermatol.*, 1970, 102:374.
- BECKER, M. H., SWINYARD, C. A.: Epidermolysis bullosa dystrophica in children. *Radiology*, 1968, 90:124.
- SCHUMAN, B. M., ARCINIEGAS, E.: The Management of Esophageal Complications of Epidermolysis Bullosa. *Digest Dis.*, 17:875, 1972.
- KRALIK, J., RAPANT, V.: University of Olomouc, Department of Surgery, Czechoslovakia, Personal Communication.

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Tumors of the Heart

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Abstract

Early surgical intervention in patients with cardiac myxomas is mandatory because of the high morbidity and mortality in unoperated patients. Because of a multicavitary origin of the myxomas, all cardiac chambers should be explored. Because of potential recurrence, the endocardial attachment (in the fossa ovalis in most instances) should be surgically removed. The problem of atrial myxomas is discussed within the context of primary and metastatic cardiac tumors.

Introduction

Prior to Pritchard's report in 1951, ante mortem diagnosis of cardiac tumors was an exception. Since this report early diagnosis made feasible the surgical removal of most primary tumors of the heart with a low mortality and morbidity. Only 0.03% of 40,000 autopsies showed primary tumors; one-half were myxomas, the others sarcomas, angiomas, rhabdomyomas, liposarcomas, and hamartomas.

Since the first attempt to remove a myxoma in 1952 by Bahnson and Newman⁴ and its first successful removal by Crafoord in 1954⁵, with the aid of extracorporeal circulation, the advances made allow safe excisional therapy of this tumor. It became of paramount importance to evaluate the natural history and clinical presenta-

tion and to make a diagnosis before irreversible complications had occurred.

Large individual series are not available; review of the cases reported since January 1968 to June 1973 in the English literature amounts to a total of 62 cases.

The overall high incidence of embolization in myxomas makes early surgical intervention mandatory.

The purpose of this paper is to report a case of left atrial myxoma and to analyze the cases reviewed in the literature.

Case Report

A 54-year-old white female was admitted to the Washington Hospital Center with a history of atypical dull chest pain provoked by exertion for the last eight years. On physical examination she had a normal PMI, a loud S1, an intermittent click along the left sternal border which could be induced by assuming different positions and which was associated with a diastolic rumble with presystolic accentuation.

An echocardiogram of the mitral valve demonstrated dense echoes between the mitral leaflet and the posterior myocardium during diastole, with an echo-free early diastolic phase. (Figure 1)

Cineangiography from a pulmonary artery injection showed, in the left ventriculogram and left atrial opacification, a filling defect moving from the left atrium to the left ventricle in diastole and back through the mitral valve in systole.

Excisional therapy was accomplished under cardiopulmonary bypass with fibrillatory cardiac arrest. Through a left atriotomy the tumor was located in this chamber, with a short stalk attached to the septal wall in the lower lip of the fossa ovalis. A portion of full thickness septal wall was removed with the base of the stalk through a right atriotomy, and the septal defect created in this way was repaired by simple suturing technique.

The patient had an uneventful recovery and was discharged in ten days. *Pathology:* The tumor measured 4 x 6 centimeters, was tan purple in color, of gelatinous consistency, with a slightly lobulated surface and with an eccentric stalk of whitish fibrous appearance 0.3 cm in diameter at the site of pedicle attachment. Microscopically the mass showed an eosinophilic myxoid stroma with multiple foci of hemorrhage, a poor cellular pattern consisting of individual and at times groups of cells which were ovoid with occasional spindling, eosinophilic cytoplasm and slightly hyperchromatic nucleus. (Figure 2)

Review of Literature: Sixty-two cases were suitable for analysis and were reviewed. Twenty-three were males and thirty-one females. The age of the patients ranged between three months

TUMORS OF THE HEART

MISPIRETA, MARSH, BACOS, DIAZ AND ABSOLON

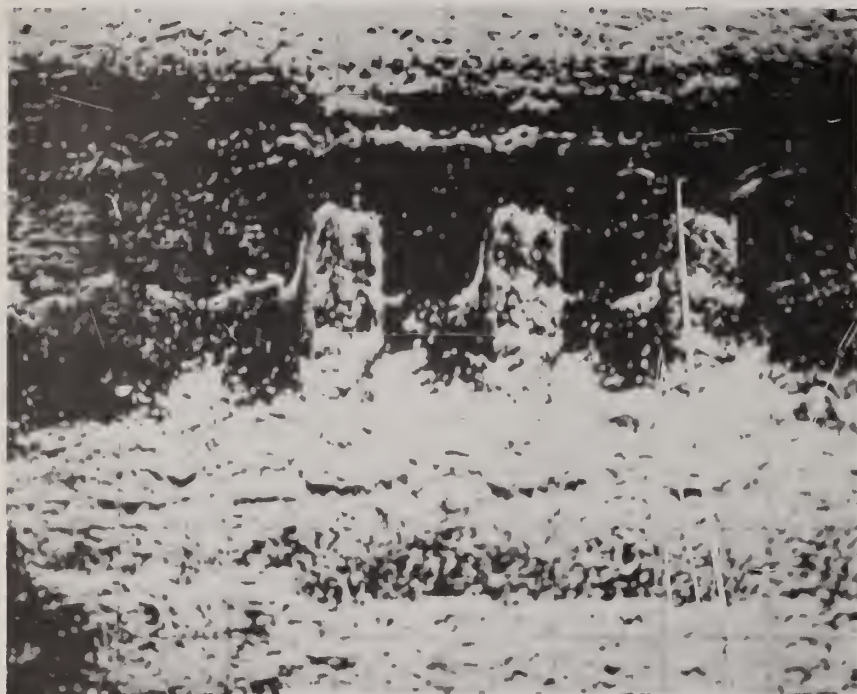


FIG. 1. Echocardiogram of mitral valve.

and 72 years, but the peak incidence was in the fifth decade of life.

The group comprised 58 benign tumors and four multiple tumors. Two tumors were malignant. Two cases of recurrent benign myxomas were encountered. (Table 1)

Of the single myxomas, 63.9% were located in the left atrium, 25% in the right atrium and 5% in the left ventricle and 5% in the right. (Table 2) Of the multiple tumors, (4) two were located in both atria, one in the right atrium and pulmonary artery; one had

multiple myxomas in the left atrium. (Table 3)

Symptomatology: The tumors with left atrial location most commonly presented with symptoms of mitral stenosis, regurgitation, or both. Forty percent presented with evidence of peripheral embolization. Other manifestations were atrial fibrillation, bacteremia and endocarditis. (Table 4)

In the patients with right atrial myxoma the presence of tricuspid stenosis or insufficiency was the commonest presentation; four patients

TABLE 1: Pathology

Single	58	Benign	60
Multiple	4	Malignant	2

Recurrent Benign 2

TABLE 2: Single Myxomas

Left Atrium	63.9%
Right Atrium	25.8%
Left Ventricle	5.1%
Right Ventricle	5.1%

TABLE 3: Multiple Myxomas

L.A. & R.A.	(2)
R.A. & P.A.	(1)
L.A.	(1)

(22.2%) had a patent foramen ovale with a right to left shunt. One of these had paradoxical tumor embolization. Pulmonary embolism was significant in 27.7%. There were six tumors in this group that showed calcification. (Table 5)

The number of patients with ventricular myxomas is not large enough to draw conclusions, but conceivably the incidence of embolization should be greater because of the higher pressures. We found three cases in the left ventricle with two instances of peripheral embolization and three in the right ventricular location with two instances of pulmonary embolization. (Tables 6 and 7)

Of the entire group 51 underwent surgery with a mortality of 9.8% and an incidence of operative embolization of 5.8%.

Discussion

A very detailed discussion of the clinical characteristics of atrial myxomas appears in the literature.⁶ Therefore, we will limit ours to some of the

TABLE 4: Symptoms in L.A. Myxomas

M.S. & M.I.	12.5%
M.S.	25.0%
M.I.	25.0%
Peripheral Embolism	40.0%
Bacteriemia & Endo- Carditis	2.5%
Atrial Fibrillation	10.0%
History of Rheumatic Fever	7.5%

TABLE 5: Symptoms in R.A. Myxomas

T.I.	16.6%
T.S.	16.6%
ASD with R→L Shunt	22.2%
Pulmonary Emboli	27.7%
Cerebral Emboli (ASD)	5.5%

TABLE 6: Presenting Symptoms in Left Ventricular Myxomas in 3 cases

Peripheral Embolism	2
Associated Rheumatic Mitral Valve Disease	1

TABLE 7: Presenting Symptoms in Right Ventricular Myxomas in 3 cases

Pulmonary Emboli	2
Pulmonic Stenosis	1
Bacteriemia + Endocarditis	1

prominent features found in our case.

As previously suggested^{7,8} the most precise non-invasive method of diagnosis is probably the echocardiographic evaluation of the mitral or tricuspid valves. In the case presented it was diagnostic. The accuracy of this technique has not yet been determined. Ninety-one percent of patients with left atrial tumors had evidence of valve obstruction manifested by pulmonary hypertension or mitral valve murmurs.⁹ Most left atrial myxomas prolapse through the mitral valve, and thus should be detected by echo techniques. Nasser¹⁰ studied six pa-

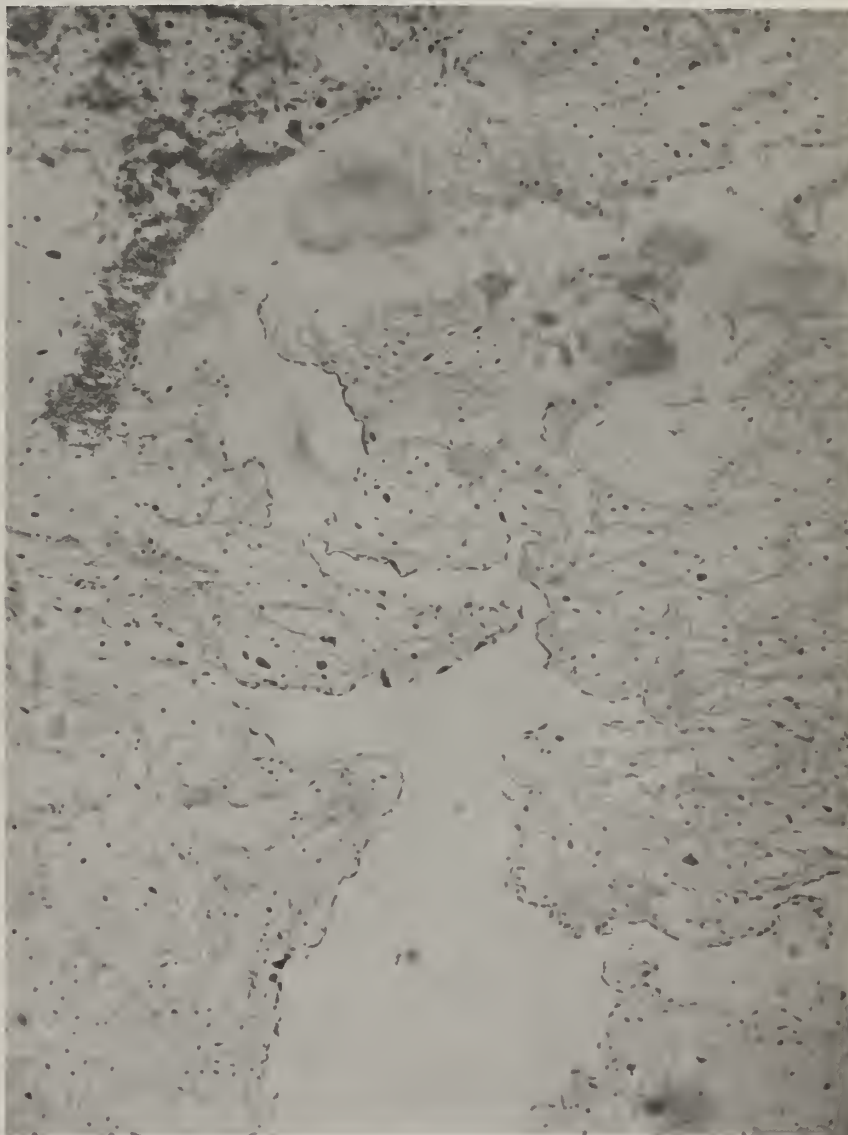


FIG. 2. Pathological picture of myxoma.

tients with myxoma of the atria, making the correct diagnosis in five. The one not diagnosed was a right atrial myxoma.

Cineangiography has been utilized for this purpose since Goldberg *et al.* demonstrated for the first time a left atrial myxoma in a three year old child.¹¹ Occasionally angiography in two planes may be necessary to dem-

onstrate the tumor.¹² Injection of the contrast material into the pulmonary artery is the technique of choice so as to avoid dislodgment of the tumor by the catheter or the powerful injection jet. Marpole reported a sudden fatal embolization during a trans-septal left atrial catheterization.¹³ Steiner recommends injecting the superior vena cava for right sided tumors, and

TUMORS OF THE HEART

MISPIRETA, MARSH, BACOS, DIAZ AND ABSOLON

pulmonary injections with follow through of the bolus of dye to left atrium or ventricle for left sided tumors.¹⁴

The surgery is safe if performed with avoidance of certain pitfalls.¹⁵ The mortality of 9.8% and the risk of operative embolization of 5.8% found in our review of the literature is certainly lower than the chance of preoperative embolization (40%).

The previous divergence of opinion regarding the exact nature of myxomas, *i.e.*, swollen thrombi versus true neoplasms, at present favors the latter. Merkow supports this view and suggests that they derive from myoid endocardial (endothelial or subendothelial) cells.¹⁶ Silverberg states that since endothelial cells, fibroblasts and smooth muscle cells were all found in the normal human atrial endocardium while smooth muscle cells are absent from the subendocardium, a tumor such as an atrial myxoma which may include all three elements would be more likely to originate from the endocardial than from the subendocardial reserve cells.¹⁷

From the data obtained from the literature, there are several aspects that deserve further discussion. The age and sex distribution is similar to others reported^{15,18} with a predominance in females in the fifth decade.

The presence of multiple tumors in one or various chambers justifies careful surgical exploration of all chambers of the heart.

The first recurrent benign tumor was reported by Gerbode¹⁹ and since then other reports suggest that removal of the attachment might be necessary. The distribution in the different chambers seems fairly consistent through the literature with about 50% of them in the left atrium, 25% in the right atrium and the remainder elsewhere.¹⁹

With respect to left atrial myxoma, it has been stated that the "classical"

presentation is the one of mitral stenosis without history of previous rheumatic fever and without fibrillation.⁶ It is of importance to note that 10% of the cases reviewed had atrial fibrillation and 7.5% gave a previous history of rheumatic fever.

Of significance in patients with right atrial myxomas is the 22.2% incidence of patent foramen ovale with a right to left shunt. It is not clear whether the manifestations of a right to left shunt makes detection easier than in patients without shunts. Myxomas of the right side with pulmonary embolization are more difficult to diagnose because of their often silent features compared to left sided myxomas and the more dramatic peripheral arterial emboli.

Calcification of myxomas was uncommon. Seven of 62 cases contained calcium and six of these were located in the right atrium and one in the left. Of the six calcified right atrial tumors, five patients required additional repair of the valve. We interpret this finding as being related with a longstanding, more silent tumor and its "wrecking ball" injury of the valve.

The overall high incidence of embolization in myxomas makes early surgical intervention mandatory.

Conclusions and Summary

Early surgical intervention in patients with cardiac myxomas is mandatory because of the high morbidity and mortality in unoperated patients. Because of a multicavitary origin of the myxomas, all cardiac chambers should be explored. Because of potential recurrence the endocardial attachment (fossa ovalis in most instances) should be surgically removed.

Bibliography of Cases Reviewed from Literature

Jan. 1968—June 1973

1. Abdur, R. T., et al.: New York State Journal of Medicine, 2996, 1970.
2. Anderson, S. T., et al.: The Journal of Thoracic and Cardiovascular Surgery, 59: 768, 1970.
3. Bahl, O. P., et. al.: Circulation, 15: 673, 1969.
4. Bigelow, G. C., et. al.: Surgery, 65: 247, 1969.
5. Bower, P. J., et. al.: The American Journal of Cardiology, 23: 592, 1969.
6. Bruno, M. S., Ober, W. B.: New York State Journal of Medicine, 2423, 1968.
7. Castaneda, A. R., Varco, R. L.: Progress in Cardiovascular Diseases, 11: 304, 1969.
8. Collins, H. A., Collins, I. S.: Annals of Thoracic Surgery, 5: 450, 1972.
9. Craig, E., Algary, W. P.: Arch. Internal Medicine, 129: 470, 1972.
10. Danta, G., Williams, D. O.: British Heart Journal, 31: 799, 1969.
11. Fleming, H. A., Stovin, P. G. I.: Thorax, 27: 373, 1972.
12. Fluck, D. C., Lopez, B. L.: Proc. Royal Society Medicine, 61: 33, 1968.
13. Ghahramani, A. R., et. al.: The American Journal of Medicine, 52: 525, 1972.
14. Glasser, S. P., et. al.: The American Journal of Medicine, 50: 113, 1970.
15. Goldschlager, A., et. al.: The American Journal of Cardiology, 30: 82, 1972.
16. Hansen, J. F., et. al.: Acta Med. Scand., 186: 165, 1969.
17. Hickie, J. B., Gibson, H.: The Medical Journal of Australia, 82, 1970.
18. Hubbard, T. F., Neil, R. N.: American Heart Journal, 81: 548, 1971.
19. Jewitt, D.: Proc. Royal Soc. Med., 64: 42, 1971.
20. Kabbani, S. S., Cooley, D. A.: The Journal of Thoracic and Cardiovascular Surgery, 65: 731, 1973.
21. Khan, M. A. R., Mujahed, M. A.: Thorax, 25: 634, 1970.
22. Kostis, J. B., Moghadam, A. N.: Chest, 58: 550, 1970.
23. Krause, S., et. al.: Chest, 60: 404, 1971.
24. Kulkarni, M., et. al.: Thorax, 24: 629, 1969.
25. Malloch, C. I., et. al.: The American Journal of Cardiology, 25: 353, 1970.
26. Mandel, M. M., Strimel, W. H.: JAMA, 214: 2154, 1970.

27. Mark, L. E.: Medical Annals of the District of Columbia, 39: 615, 1970.
28. Marks, I. N.: British Medical Journal, 3: 537, 1968.
29. Marpole, G. F., et. al.: American Journal of Cardiology, 23: 597, 1969.
30. Marshall, W. H., et. al.: Radiology, 93: 815, 1969.
31. Martin, C. E., et. al.: American Heart Journal, 78: 245, 1969.
32. Mundth, E. D., et. al.: The Annals of Thoracic Surgery, 5: 255, 1968.
33. Price, D. L., et. al.: Arch. Neurol., 23: 558, 1970.
34. Ramsey, H. W., et. al.: Arch. Internal Medicine, 124: 206, 1969.
35. Schattenberg, T. T.: Mayo Clin. Proc., 43: 620, 1968.
36. Spencer, W. H.: Arch. Internal Medicine, 128: 787, 1971.
37. Steinke, W. E., et. al.: Pediatrics, 49: 580, 1972.
38. Talley, R. C., et. al.: The American Journal of Medicine, 48: 256, 1970.
39. Trinkle, K., et. al.: The Journal of Thoracic and Cardiovascular Surgery, 61: 765, 1971.
40. Vera, C. A., et. al.: Dis. Chest, 56: 162, 1969.
41. Wilcox, B. R., Carter, J. M.: Annals of Surgery, 173: 131, 1971.
42. Yacoub, M. H., et. al.: The American Journal of Cardiology, 27: 442, 1971.
43. Yarnell, P. R., et. al.: Stroke, 2: 35, 1971.
44. Yipintsol, T., et. al.: Dis. Chest, 52: 828, 1967.

References

1. PRICHARD, R. W.: Tumors of the heart. Arch. of Path., 1951, 51:98.
2. GRIFFITHS, C. C.: Progress Card. Vas. Dis., 1965, 7:465.
3. HEATH, D.: Pathology of cardiac tumors. Am. J. Cardiol., 1968, 21:315.
4. BAHNSON, H. T., NEWMAN, E. V.: Diagnosis and surgical removal of intracavitary myxoma of the right atrium. Bull. Johns Hopkins, 1953, 93:150.
5. LINDSKOG, G. E., LIEBOW, A. A., GLENN, W. W.: Thoracic and cardiovascular surgery with related pathology. New York, Appleton Century Crafts, 1962, p. 927.
6. HARVEY, W. P.: Clinical aspects of cardiac tumors. Am. J. Cardiol., 1968, 21:328.
7. POPP, R. L., et. al.: Ultrasound for the diagnosis of atrial tumor. Ann. Int. Med., 1969, 71:785.
8. WOLFE, S. B., et. al.: Diagnosis of atrial tumors by ultrasound. Circulation, 1969, 39:615.
9. GOODWIN, J. F.: Diagnosis of left atrial myxoma. Lancet, 1963, 1:464.
10. NASSER, W. K., et. al.: Atrial myxoma. Am. Heart J., 1972, 83:810.
11. GOLDBERG, H. P., et. al.: Myxoma of the left atrium. Diagnosis made during life with operative and post mortem findings. Circulation, 1952, 6:762.
12. WISE, J. R.: Atrial myxoma and angiocardiology. Ann. Int. Med., 1970, 72:756.
13. MARPOLE, D. G. F., et. al.: Atrial myxoma, a continuing diagnostic challenge. Am. J. Cardiol., 1969, 23:597.
14. STEINER, R. E.: Radiological aspects of cardiac tumors. Am. J. Cardiol., 1968, 21:344.
15. KABBANI, S. S., COOLEY, D. A.: Atrial myxoma, surgical considerations. J. Thorac. Cardiovasc. Surg., 1973, 65:731.
16. MERKOW, L. P., et. al.: Ultrastructure of a cardiac myxoma. Arch. Path., 1969, 88:390.
17. SILVERBERG, S. G., KAY, S.: Ultrastructure of a cardiac myxoma. A.J.C.P., 1970, Oct.:650.
18. MILLER, J. I., et. al.: Primary cardiac tumors. Surgical considerations and results of operation. Supplement I to Circulation, 1972, Vols. XLV and XLVI:134.
19. GERBODE, F., et. al.: Surgical management of tumors of the heart. Surgery, 1967, 61:94.
20. GHAHRAMANI, A. R., et. al.: Left atrial myxoma. Hemodynamic and phonocardiographic features. Am. J. Med., 1972, 52:525.

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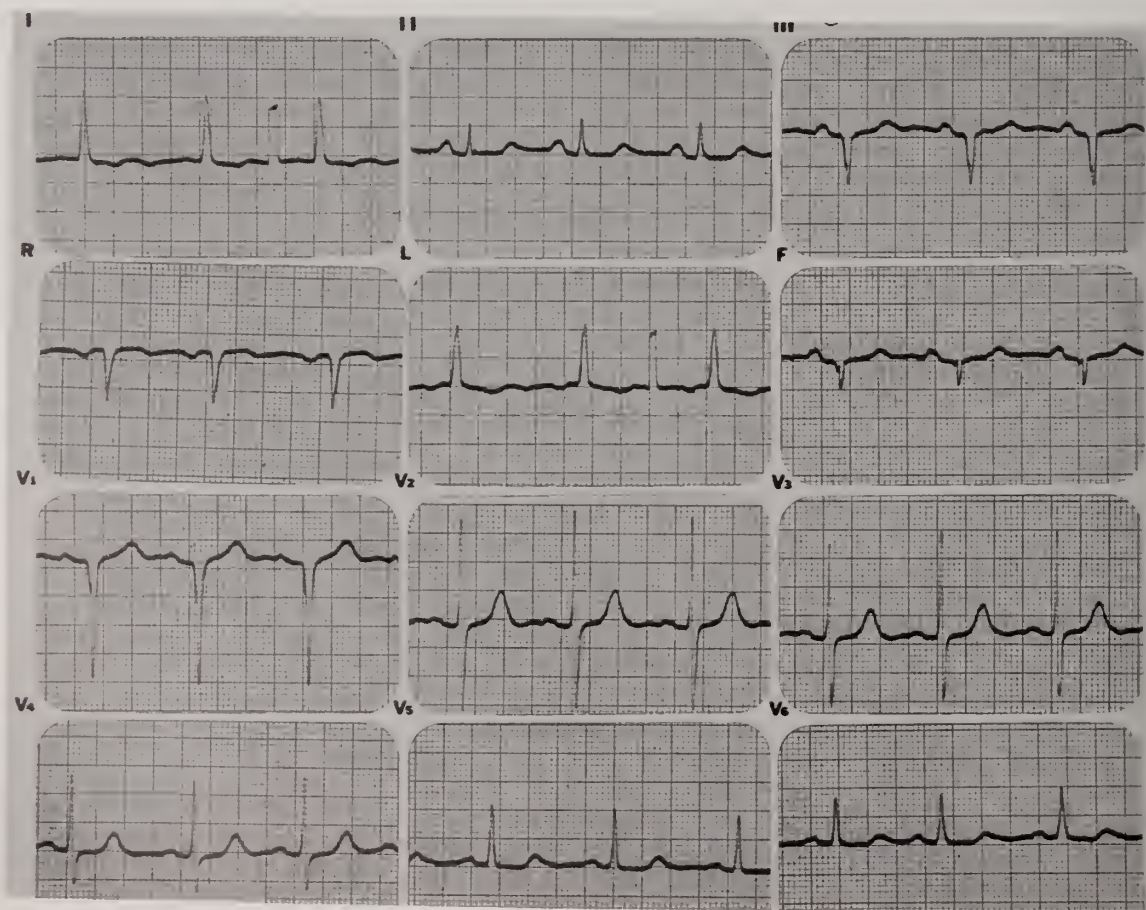
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ECG PROBLEMS

HISTORY: A 26-year-old white female with a heart murmur since childhood. It has always been considered insignificant. No significant cardiac symptoms. Exam shows no cardiac enlargement. Second sound is loud and palpable in the second interspace at the sternal edge. There is questionable splitting of the second sound and the second right interspace. First sound is normal. Grade II-III/VI early and mid systolic murmur loudest along the left sternal edge. No diastolic murmurs. Chest X ray (4 views): normal.

(for diagnosis see page 262)



The Morphology, Physiology and Therapy of Mitral Valve Disease with Giant Left Atria

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Abstract

This report concerns a patient with a long standing history of mitral valve disease leading to a giant left atrium with a capacity of 2700 ml., treated with a disc mitral valve prosthesis. It is one of the largest with survival after valve replacement reported in the literature. This rare entity, accounting for only 0.3% of patients with rheumatic heart disease and 12% of patients undergoing surgery for rheumatic mitral valve disease, was discussed. The anatomy, physiology and therapy were reviewed in the context of a literature review.

The distinct improvement in the cardiac status of patients with mitral valve replacement appears to support surgical intervention as the treatment of choice.

Introduction

Most authors define a giant left atrium on basis of radiological appearance. The left atrium must outline both the right and left border of the heart and approximate the right chest wall.¹ Also referred to as aneurysmal dilatation, it is rarely associated with rheumatic or congenital mitral valve disease, accounting for only 0.3% of mitral valve disease.

The first reported case was in 1901 by Fenton and Owen. The left atrial

capacity was reported to be 900 ml.² The largest left atrium (measured at autopsy) had a volume of 3000 ml. It was described by Minkowski.³

The present report concerns the review of the literature of this rare entity and evaluation of a 40 year old man operated on at the Washington Hospital Center by one of us (K.B.A.).

Case History

Mr. L. M. is a 40-year-old white man who was first noted to have a heart murmur at age ten, following an attack of acute rheumatic fever at age nine. He remained asymptomatic till 1960 when, at 28, he developed a chronic cough with occasional hemoptysis. That fall he was in frank congestive heart failure with syncopal attacks treated with digitalis, but his condition improved.

Upon admission to the National Institutes of Health he was found to be dyspneic on going up six or seven steps or on walking one or two blocks. The physical examination showed murmurs of mitral stenosis and regurgitation, with atrial fibrillation. Cardiac catheterization showed a normal pulmonary pressure of 28/19 mm.Hg with a mean pressure of 24 mm.Hg and no gradient across the pulmonary valve. The mean left atrial pressure was 15 mm.Hg (Z-12 mm.Hg, V-27 mm.Hg). The left ventricular

pressure was 110/9 mm.Hg. The insufficient mitral valve area was calculated at 2.06 cm². The cardiac output was measured at 6.07 L/m; the cardiac index at 3.53. There was no evidence of aortic valve dysfunction or left heart failure.

Despite medication with digoxin, 0.25 mg twice a day, he continued to have episodes of paroxysmal dyspnea, necessitating numerous admissions and medication with diuretics.

In January 1973 he was admitted to the Washington Hospital Center emergency room with history of recent onset of paroxysmal nocturnal dyspnea.

The prognosis in patients with giant atria is presently speculative. Prosthetic mitral valve replacement appears the treatment of choice.

Physical Examination

Mr. L. M. was a cachectic looking white man with a weight of 52 Kg. and a height of 5'6".

His pulse was 110/min, irregularly irregular both in volume and rhythm. His blood pressure was 110/70. There was no clubbing or pedal edema evident. His jugular venous pressure

MITRAL VALVE DISEASE WITH GIANT LEFT ATRIA

QAZI, MISPIRETA, RUSSO, BACOS AND ABSOLON

was 15 cm. of water with prominent "c" and "v" waves. A thrusting cardiac apical pulse was felt in the sixth intercostal space, 2 cm. lateral to the midclavicular line, and an additional parasternal heave suggested biventricular hypertrophy. A loud first sound and normal second aortic and pulmonic sounds were audible. An opening snap was heard 0.08 sec. after the second heart sound at the left sternal border. A grade III/VI apical diastolic rumble, a grade IV/VI parasystolic murmur at the left sternal border, and a grade I/VI decrescendo diastolic blow at the left sternal border were also appreciated.

Abdominal examination revealed prominent superficial veins forming a *caput medusae*. (Figure 1) The liver, 14 cm. in span, was palpated 4 cm. below the right costal margin. The spleen was not felt.

Laboratory findings included an ASO titre of 250 Todd units. The

serum was negative for C-reactive protein. The electrocardiogram showed atrial fibrillation with a ventricular response of 72-150/min.; evidence of left atrial enlargement and digitalis effect.

The chest X-Rays left no doubt as to the massive left atrial enlargement (Figure 2a).

Cardiac Catheterization (Table I)

A left atrial mean pressure of 22 mm.Hg and a "v" wave pressure of 25 mm.Hg was revealed, as shown in Table 1. The pulmonary artery pressures showed an elevated diastolic pressure of 21 mm.Hg and a mean of 23 mm.Hg. The right ventricular pressures were marginally elevated, 35 mm.Hg systolic and 6-12 mm.Hg diastolic. The right atrial mean pressure was 12 mm.Hg, and the "v" wave pressure was 14 mm.Hg. The left ventricular and aortic pressures were unremarkable.

The left ventricular end-diastolic volume was 137 ml. with a stroke volume of 71 ml. and end-systolic volume of 66 ml.

In view of the above findings it was felt that the predominant lesion was mitral stenosis with some mitral incompetence.

By subtracting the total estimated blood volume of the patient from the measured blood volume, a left atrial volume of 2700 ml. was estimated.

Management

After vigorous diuretic therapy and digitalization, the patient was operated on through a midline sternotomy incision. Upon incision, the pericardium was entered; a massive left atrium was found to surround the cardiac ventricles, while the right atrium was riding atop it (Figure 3). The compression of the inferior vena cava by the large atrium clearly produced the venous collaterals of the *caput medusae* type.

After the patient had been placed on the cardio-pulmonary bypass, the left atrium was entered through a vertical atriotomy posterior to the interatrial groove. Interestingly, no clots or thrombi were found in the left atrium, despite its enormous size and the 2700 ml. of blood that was aspirated. The atrium measured approximately 20 X 10 X 10 centimeters in the collapsed state. The mitral valve was grossly scarred and misshapen with a fishmouth measuring approximately 2 sq. cm. in area. The valve was excised and a Beall type prosthetic valve was sutured in place with interrupted 2-0 Tevdek sutures over Teflon pledgets. (Figure 2b).

The postoperative course was uneventful. The patient was continued on digoxin medication and after one week of coumadin anticoagulation was stopped and the patient placed on acetyl salicylate, 10 gr. daily.



FIG. 1. "Caput medusae" secondary to compression of the inferior vena cava by a giant left atrium.



FIG. 2A. Preoperative: The massive left atrium is seen to form the right border of the heart and part of the left border.

The patient's orthopnea was relieved, and he resumed an active life and physical activity.

The patient was readmitted four months post-operative for re-evaluation and cardiac catheterization. He was at this time asymptomatic, taking 0.25 mg. digoxin daily. His weight had increased by 4 Kg. to 56 Kg. His pulse rate was 68/min. irregularly irregular, and blood pressure, 110/70. His heart was still enlarged, the apex being palpable in the sixth intercostal space in the anterior axillary line. A grade II/VI ejection systolic murmur was audible at the left sternal border. No regurgitant murmurs were detected.

Blood volume studies were done. By extrapolation the volume of the left atrium was estimated at 500 ml.—a decrease of 2200 ml. in spite of only minor decrease in size of the cardiac silhouette on the chest X-Ray.

The findings at cardiac catheterization are shown in Table 1. The diastolic pressures in the right ventricle and pulmonary bed had decreased. Pressures in the left atrium had also fallen. The prosthesis was found to be competent.

TABLE I Pre and Postoperative Catheterization Data

	RA	RV	PA	LA	LV	Left Atrium
Pre-op	14 (1)	3 1-1	3 1-1	5 (1)	13 0-16	2700 ml
Post-op	11 (1)	2 0-1	3 1-1	1 (1)	13 0-1	500 ml



FIG. 2B. Postoperative: Valve prosthesis in mitral position with some decrease in size of left atrium.

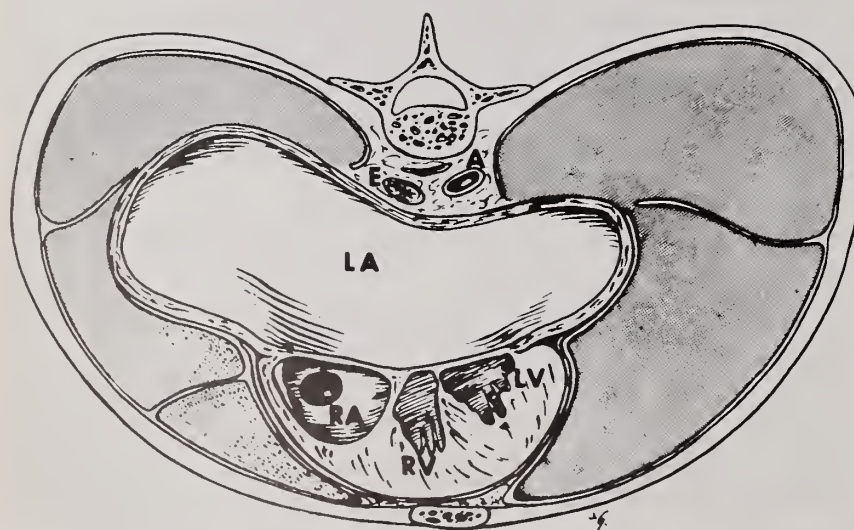


FIG. 3. Schematic presentation of anatomic distortion produced by a giant left atrium.

Discussion (Table II)

The therapeutic approach to mitral valve disease associated with giant left atria has changed in recent years. Prostheses have replaced mitral commissurotomies and valvuloplasties; the initial enthusiasm for left atrial plication or resection of the left atrial wall has waned, there being no evidence that this procedure is of benefit.

Kent and his colleagues reported five cases with predominantly mitral stenosis treated with mitral commissurotomy. There was one death.⁴ DeSanctis reported on one patient treated with commissurotomy leading to mitral insufficiency and one patient treated with insertion of a Starr-Edwards mitral prosthesis. The latter died in the early postoperative period of low output syndrome and of lower extremity gangrene.⁵ Knudsen *et al*, reported on three patients, two of whom had a Starr-Edwards prosthesis and one an aortic homograft valve. The result was relief of congestive heart failure and a return to active life for the former two.⁶ In 1967 Johnson *et al* reported a series of 17 patients who underwent plication of the left atrium; sixteen patients had a Starr-Edwards valve replacement.⁷

Plaschkes and his colleagues reported the most experience with giant left atria. In 14 out of 18 patients the valve was replaced in nine with a Kay Shirley disc valve, and in five with an aortic heterograft.¹ In three patients a tricuspid annuloplasty was added. Three patients had both the tricuspid and mitral valve replaced, two with disc valves and one with aortic heterografts. One patient had a triple valve replacement performed. There were three hospital deaths (16.6% mortality) and two later deaths from systemic emboli, giving a total cumulative mortality of 27.7%. Thirteen survivors have been under observation for up to three and one-half years. Twelve were

TABLE II Literature Review—Giant Left Atria

AUTHOR	YEAR	NO.	PROCEDURE	POSTOP COURSE	MORTALITY
Venner	1959	1	Mitral valvotomy	Relieved of congestive heart failure.	
Kent	1956	5	Mitral valvotomy	4 had favorable course 5-7 months postop.	1 died of intractable (R) heart failure
DeSanctis	1959	2	1 Mitral valvotomy 1 Mitral replacement	Splenic and (L) renal emboli.	Died after emergency appendectomy Died after insertion of Starr valve prosthesis
Guest	1965	1	Mitral replacement	Bilateral symmetrical gangrene.	Died 5 weeks postop
Johnson	1967	17	16 Mitral replacement and plication 1 Plication only	11 patients did well.	6 deaths. (1 pulmonary embolus, 1 hemorrhage at thoracotomy, 4 died of low output syndrome on 3rd postop day on the average)
Piwnica	1967	29	21 Mitral replacements & Annuloplasties	Information not available.	7 deaths. (6 after valve replacement, 1 after annuloplasty)
Knudsen	1969	3	Mitral replacement	2 relieved of congestive heart failure.	1 died of cerebrovascular accident 2 hours postop following loss of anticoagulant control.
Plaschkes	1970	18	Mitral replacement	7 said to be improved. 4 did very well. 1 unimproved, 1 late systolic murmur due to mitral valve insufficiency.	3 hospital deaths (2 ventricular fibrillation, 1 low output syndrome) 2 late deaths (1 from cerebral embolus and 1 with cerebral and coronary emboli)

clinically and hemodynamically improved.

The cause of the extreme dilatation of the left atrium in mitral disease has not yet been established. While the overall incidence of giant left atria is only 0.3% in cases with rheumatic heart disease, it is found in some 12% of patients undergoing surgery for rheumatic mitral valve disease.¹ Degenerative changes in the wall of the left atrium was postulated but not established as a definite cause. Fibrosis found on histological examination of the left atrial wall in our patient is not of greater magnitude than in patients with smaller size atria. No Aschoff's bodies have been reported in the atrial

wall in any of the cases reported. Left atrial pressure bears no relationship to the size of the chamber.

Mitral stenosis or regurgitation may be present; usually there is a combination of the two, such as in our patient. In a series of 14 cases presented by Kent *et al*, only two had pure mitral stenosis, and two, pure mitral regurgitation.⁴

Anatomical Considerations

Figure 2 shows the extraordinary dilatation of the left atrium, from a normal average capacity of 140 ml. to a volume of up to 3000 ml. The anatomical alterations produced are

worthy of note. There is initial enlargement to the right. Located normally just under the tracheal bifurcation, the left atrium is the most posterior and superior of the cardiac chambers. Anteriorly, it is partially bounded by the great vessels arising from the base of the heart. To the left, anteriorly and inferiorly, is the left ventricle, which with the biventricular enlargement, characteristically present in these patients, usually rotates in a clockwise fashion and is displaced anteriorly. The descending aorta and the spine form an additional barrier to leftward enlargement. Further dilatation may produce compression and displacement of the inferior vena cava, as seen in our patient.

MITRAL VALVE DISEASE WITH GIANT LEFT ATRIA

QAZI, MISPIRETA, RUSSO, BAÇOS AND ABSOLON

Further enlargement of the left atrium proceeds to the left, ultimately lifting the heart as a crown on a cushion. The esophagus is compressed posteriorly, producing dysphagia, loss of weight and emaciation, as observed by the authors. In some cases dysphagia may be extreme. Nichols and Ostrum reported on a woman in whom a feeding gastrostomy was placed because a suspicion of esophageal neoplasm was entertained.⁸

The carinal angle is widened with displacement of the adjacent bronchi. Atelectasis secondary to compression of a bronchus or lung parenchyma is sometimes seen.

Bone erosion is rare, but was reported in two cases by Ashworth and Jones. In one of their patients the atrium had eroded the fifth through the ninth vertebra.⁹

Compression of the pulmonary artery leading to its dilatation and its pressing on the left recurrent laryngeal nerve to produce hoarseness were named Ortner's syndrome.⁵

The diagnostic hazards may be varied. In the first case reported in 1901, a thoracentesis through the right chest to evacuate a supposed pleural effusion on the basis of findings on physical examination produced a gush of blood which led to the correct diagnosis.²

The prognosis in patients with giant atria is presently speculative. As to the survival the long term effects of mitral valve replacement are not available. The quality of life is undoubtedly improved.

3. MINKOWSKI, O.: Demonstration eines Herzens mit ungewöhnlich starker Dilatation der Vorhöfe. *Munchen Med. Wsch.*, 1904, 51:182.
4. KENT, E. M., FISHER, D. L., FORD, V. B., NEVELLE, J. F.: Mitral Valve Surgery and Left Heart Catheterization in Giant Left Atrium. *Arch. Surg.*, 1956, 73:503.
5. DeSANCTIS, R. W., DEAN, D. C., BLAND, E. F.: Extreme Left Atrial Enlargement. Some Characteristic Features. *Circulation*, 1964, 29:14.
6. KNUDSEN, D. F., DAILY, O. P., STINSON, E. F., SHUMWAY, N. E.: Surgical Treatment of the Gigantic Left Atrium. *Surg. Gynec. & Obstet.*, 1969, 128:565.
7. JOHNSON, J., DANIELSON, G. L., MacVAUGH, H., JOYNER, C. R.: Plication of Giant Left Atrium at Operation for Severe Mitral Regurgitation. *Surgery*, 1967, 61:118.
8. NICHOLS, C. F., OSTRUM, H. W.: Unusual Dilatation of the Left Auricle. *Am. Heart J.* 1933, 8:205.
9. ASHWORTH, H., JONES, A. M.: Aneurysmal Dilatation of the Left Auricle with Erosion of the Spine. *Brit. Heart J.* 1946, 8:207.

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References

1. PLASCHKES, J., BORMAN, J. B., MERIN, G., MILWIDSKY, H.: Giant Left Atrium in Rheumatic Heart Disease: *Ann. Surg.*, 1971, 174:194.
2. OWEN, I. O., FENTON, W. J.: A Case of Extreme Dilatation of the Left Auricle of the Heart. *Clin. Soc. Trans.*, 1901, 24:183.

Physiological Rationale for the Clinical Use of Low Output Pacemakers

NICHOLAS P.D. SMYTH, M.D., JOHN M. KESHISHIAN, M.D., NORMAN R. BAKER AND PETER TARJAN, PH.D.

Abstract

Prolongation of battery life in cardiac pacers is the most important goal in pacing today. It has been known for many years that the output of conventional cardiac pacers is unnecessarily high. A study of stimulating thresholds has been made in 91 patients at the time of initial implant and 60 of these patients at the time of first pulse generator replacement, and 16 of the same patients at the time of the second replacement. Electrodes of two different sizes were used. The results showed that the thresholds were lower with the smaller electrode and with both electrodes were remarkably stable and lower than is commonly thought. The study indicates that the combination of a small electrode and reduced pulse generator power and output is a logical way to minimize current drain on the battery and prolong the life of the pacemaker pulse generator.

Introduction

It has been known for many years that the output of conventional cardiac pulse generators was unnecessarily high. Output levels of around 10 ma. and 6.5 v. have been standard since the early days of permanent pacing. Manufacturers have been reluctant to reduce output because of early problems with

We began measuring stimulating thresholds in clinical pacemaker implantation using both constant current and constant voltage sources at varying pulse widths. . . .

"exit block" due to rise on the threshold of cardiac excitability to levels exceeding the output of the pulse generator.¹

Improvements in lead design, specifically the reduction in surface area of the electrode² have led to the phenomenon of exit block and high thresholds becoming extremely rare.

It seemed obvious to us and to others³ that stable pacing should be possible with lower current output from the pulse generator with resultant longer life for the unit.

The significance of pulse width in relation to stimulating threshold is well known to all in the laboratory. We therefore began measuring stimulating thresholds in clinical pacemaker implantation using both constant current and constant voltage sources at varying pulse widths, so that strength duration curves could be derived for each.⁴

Materials and Methods

A variable parameter external pacemaker was used for the measurement of stimulating thresholds. The pacemaker could be used in either the constant current or the constant voltage mode. In each case, the pacing electrode was coupled to the electronics through a 100 microfarad coupling capacitor. In contrast to other pacers the "Synchroc" * in the constant voltage mode is not a capacitive discharge system but a true constant voltage source, which maintains the set voltage between the electrodes for the duration of the pulse. All thresholds were measured by reducing output, either constant current or voltage, until capture was lost. Clinically this is the only practical method. Rising output thresholds are not feasible in a patient with a very slow intrinsic rate. The thresholds were measured first in milliamperes and then in volts at pulse widths of 0.5, 1.0, 1.5, 2.0 and 2.5 milliseconds. A complete series of these measurements was routinely carried out at the time of implantation of a new pacemaker and replacement of an old one.

For uniformity only those patients with Cordis 4 mm. or 2 mm. tip electrodes are included in this study. There were eighty patients with the former and eleven with the latter. In

RATIONALE FOR CLINICAL USE OF PACEMAKERS

SMYTH, KESHISHIAN, BAKER AND TARJAN

all these patients early model R-wave synchronous pulse generators (series 129 "Ectocors",*), were used. Since we had established from our own data a 50% failure rate at 21.5 months for these units, all replacements in this series were elective at 21 and 42 months.

There were ninety-one patients in the initial implant group. Sixty of these patients were in the first replacement group at 21 months, and 16 of the same patients were in the second replacement group at forty-two months. A total of 1,670 individual threshold measurements were made in the 167 procedures on ninety-one patients.

The resultant values were averaged and expressed as strength duration curves for current and voltage. Since the pulse width was also known, theoretically energy values could have been derived and expressed in micro-joules—a concept more popular in Europe. However, since the current and voltage thresholds were not measured simultaneously, accurate energy values could not be obtained and no attempt was made therefore to plot these results.

All threshold measurements were, of course, unipolar. The indifferent electrode (anode) was an Elgiloy disc placed in the wound. It measured 3.5

cm. in diameter and 3 mm. thick. Its surface area was 25 cm.² The surface area of the 4 mm. electrode, also of Elgiloy, (cathode) was 0.295 cm.² and the 2 mm. electrode was 0.175 cm.²

Results

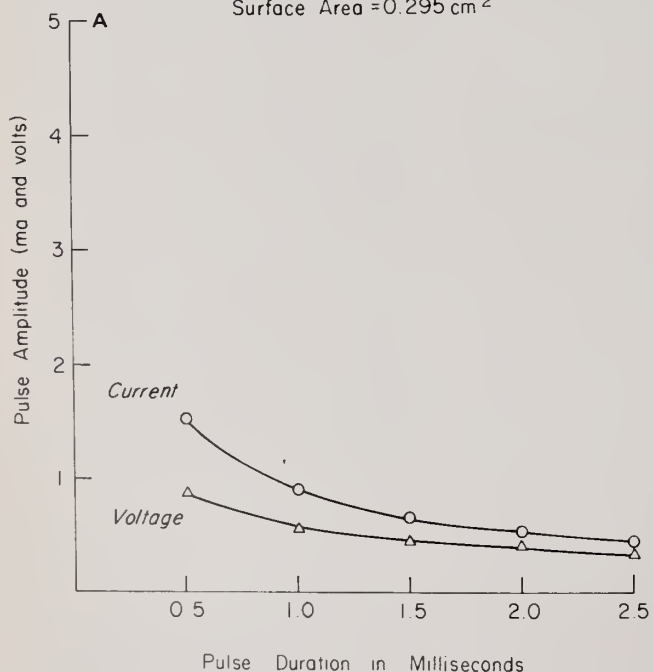
The values obtained at the time of initial insertion are shown in Figure 1. It can be seen that the current thresholds are lower for the 2 mm. electrode but there is little difference in the acute voltage threshold between the 2 mm and the 4 mm. electrode.

The same values are shown at twenty-one months in Figure 2 and at forty-two months in Figure 3. The

ACUTE VENTRICULAR THRESHOLDS

80 PATIENTS

4mm Tip Elgiloy Electrode
Surface Area = 0.295 cm²



ACUTE VENTRICULAR THRESHOLDS

II PATIENTS

2mm Tip Elgiloy Electrode
Surface Area = 0.175 cm²

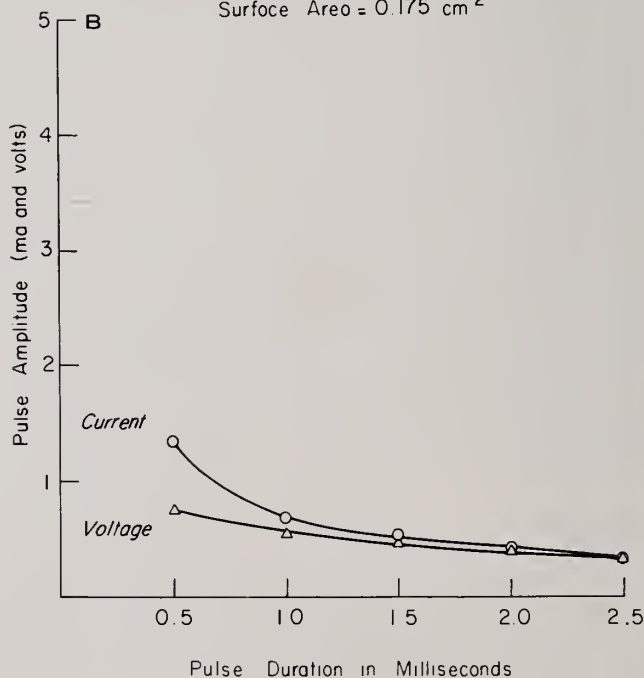


FIG. 1. A. Strength duration curves for "acute" current and voltage threshold values plotted for the 4 mm. tip Cordis electrode and: B., for the 2 mm. tip Cordis electrode, at time of initial pacemaker implantation.

lower thresholds with the 2 mm. electrode are more obvious in the chronic studies. The thresholds are about three times the initial values at twenty-one months and remain very stable with very little rise between twenty-one and forty-two months. They are also, at each time, significantly below the output of a standard pulse generator.

It seemed clear that the current output of a pulse generator could be significantly reduced with a resultant increase in the longevity of the unit. (Figure 4).

The Cordis Corporation began to produce several years ago, for investigative work, pulse generators with pulse widths of 1.0 millisecond and

outputs of 7.5 milliamperes and 5.0 milliamperes instead of the conventional 10 milliamperes and 1.5 milliseconds. We then adopted the policy of inserting a standard output unit initially. If the threshold was less than 4 ma. at the time of replacement at a pulse width of 1.0 millisecond, corresponding to that of the implantable unit, we used a 5 ma output unit for replacement. If it was less than 6 ma. we used a 7.5 output unit. Almost all thresholds were less than 4 ma.

In three patients this change yielded an extra dividend. These patients had chronic intermittent pacing of the diaphragm. Since cardiac pacing was stable we had done nothing to correct

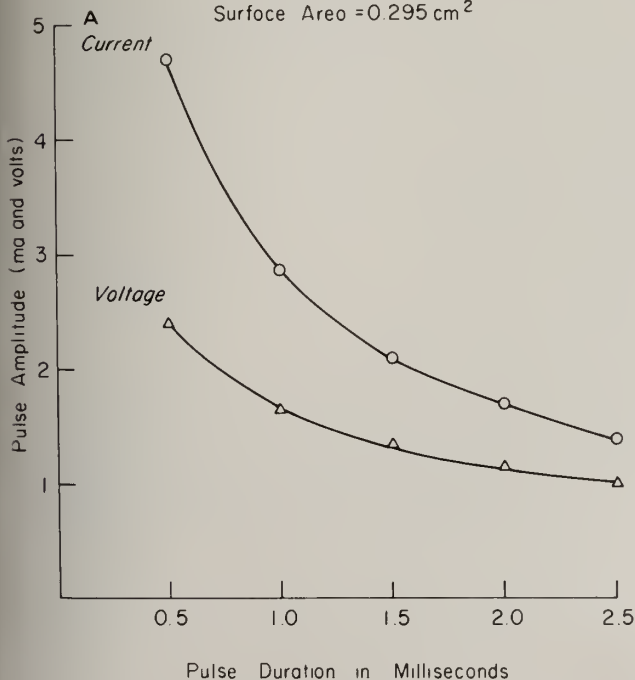
this. In each patient the threshold for pacing the diaphragm was 7 ma. and the use of a 5 ma. unit completely eliminated this annoying complication while maintaining stable cardiac pacing.

More recently the entire concept of matching the pulse generator output to the cardiac stimulating threshold has been neatly packaged in the Omnicor Series, in which the output as well as the rate of each unit can be programmed non-invasively using coded bursts to electromagnetic signals from an adjustable external programmer. When using a Cordis pacer we now insert the unit at the desired rate and "high" output (9 ma.). One

CHRONIC VENTRICULAR THRESHOLDS (21 mos)

56 PATIENTS

4mm Tip Elgiloy Electrode
Surface Area = 0.295 cm²



CHRONIC VENTRICULAR THRESHOLDS (21 mos)

4 PATIENTS

2mm Tip Elgiloy Electrode
Surface Area = 0.175 cm²

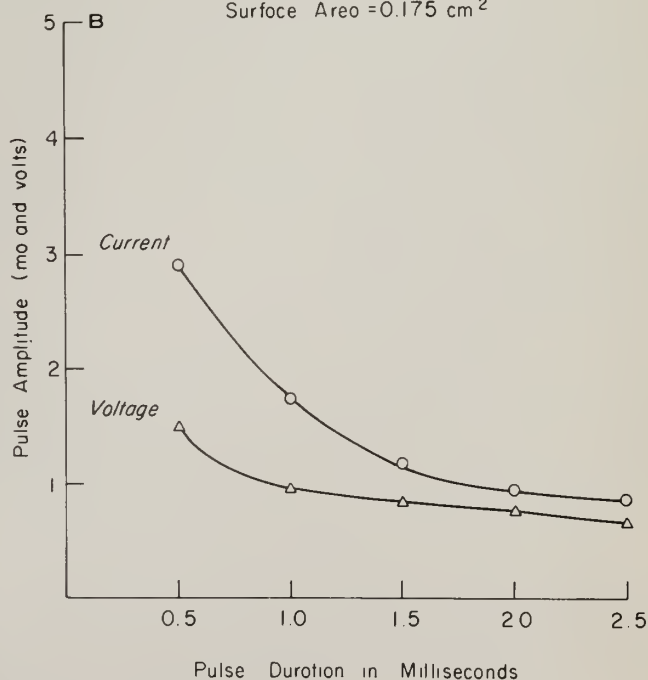


FIG. 2. "Chronic" threshold values from the same patient group, plotted similarly, at time of elective replacement of the pulse generator 21 months post-operatively: A., for the 4 mm. tip electrode and B., for the 2 mm. tip electrode.

RATIONALE FOR CLINICAL USE OF PACEMAKERS

SMYTH, KESHISHIAN, BAKER AND TARJAN

month post-operatively the output is stepped down to one setting above the lowest at which pacing is possible. In our experience with the 2 mm. electrode this is invariably the "low" setting (4 ma.). In almost all cases pacing is possible at the "test" setting (2.3 ma.) but we have not routinely left the pulse generator at this low setting.

Conclusion

The combination of a small electrode and a lowered pulse generator output is a logical way to minimize the drain on the battery and should greatly extend the life of a conventionally powered pulse generator. This is perhaps the most important goal in pacing today.

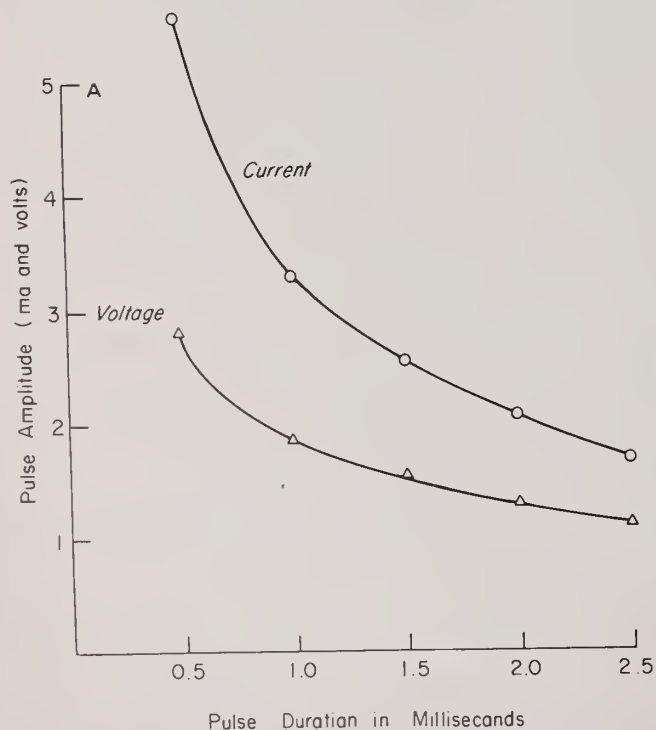
References

1. PRESTON, T. A., JUDGE, R. D., BOWERS, D. L., MORRIS, D. D.: Measurements of Pacemaker Performance. *American Heart Journal* 1966, 71:92.
2. FURMAN, S., PARKER, B., ESCHER, D. J. W., SOLOMON, N.: Endocardial Threshold of Cardiac Response as a Function of Electrode Surface Area. *J. Surg. Res.* 1968, 8:161.
3. CENTER, S., TARJAN, P.: The Clinical Application of Low-Output Pacemakers. *J. Thor. and Cardiovas. Surg.* 1972, 64:6.
4. SMYTH, N.P.D. BOIVIN, M., BACOS, J. M., KELLER, J. W.: A Modified Variable Parameter Cardiac Pacer. *Chest* 1970, 57:3.

CHRONIC VENTRICULAR THRESHOLDS (42 mos.)

14 PATIENTS

4mm Tip Elgilay Electrode
Surface Area = 0.295 cm²



CHRONIC VENTRICULAR THRESHOLDS (42 mos.)

2 PATIENTS

2mm Tip Elgilay Electrode
Surface Area = 0.175 cm²

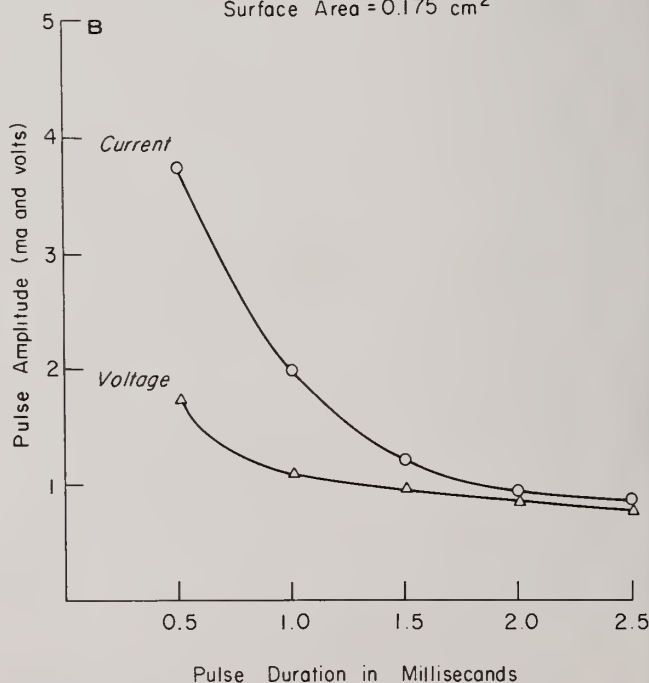


FIG. 3. "Chronic" threshold values for some of the same patients at the time of second elective replacement of the pulse generator: A., for the 4 mm. tip and B. for the 2 mm. tip.

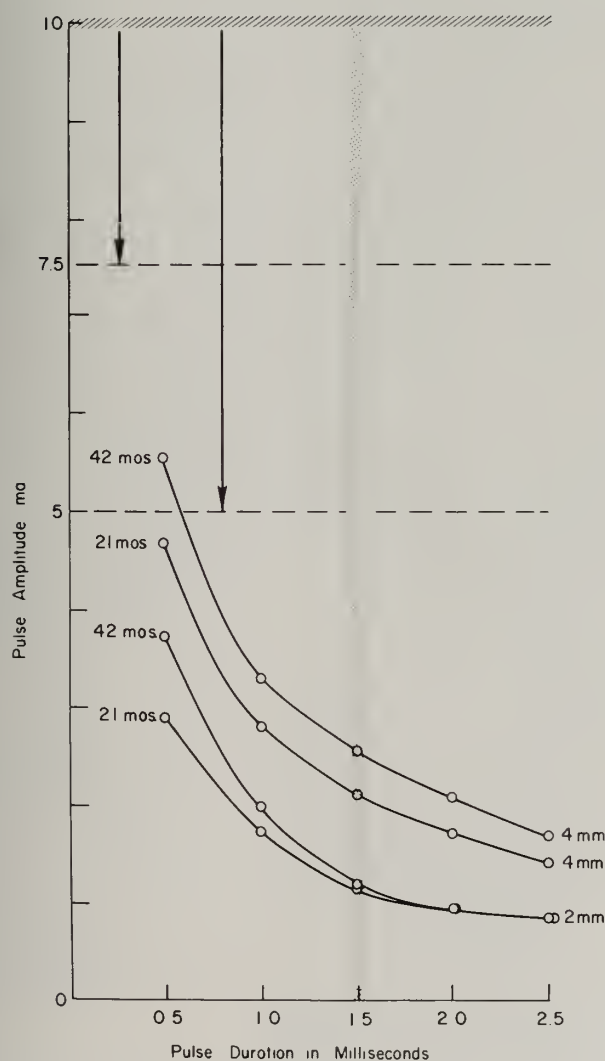


FIG. 4. Average current threshold values plotted as strength duration curves for the 4 mm. and the 2 mm. tip electrodes at 21 and 42 months post-operatively. The output of the standard unit is shown by the crosshatched bar, and the pulse width by the stippled bar. It is obvious that there is a substantial safety margin whether the current output is reduced to 7.5 or even 5.0 ma. at a pulse width of 1.0 millisecond.

* Cordis Corp. Miami Fla.

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Supported by the Potomac Fund for Cardiovascular Research, Washington, D.C.

VIEW BOX

(from page 236)

DIAGNOSIS: Hodgkins disease

The PA and lateral chest radiographs show a large cavitating mass in the left lower lobe. No pleural effusion but bilateral asymmetrical hilar and paratracheal lymph adenopathy.

About 90% of patients with Hodgkins lymphoma have intra-thoracic involvement during their disease. Usually this involves the hilar and paratracheal nodes. In about 30% there is pleuro-pulmonary involvement but almost never without nodal involvement. Most commonly it is direct extension from nodes into the lung parenchymae. Parenchymal masses with or without cavitation can occur and these often are in the lower lobes.

*Edited by Gunther J. Augustin, M.D.
Senior Attending Radiologist
Washington Hospital Center
Washington, D.C.*

ECG PROBLEMS

(from page 250)

INTERPRETATION:

1. Distortion of initial and early forces compatible with corrected transposition of the great vessels.
2. ST-T changes secondary to (1).

Cardiac catheterization demonstrated congenitally corrected transposition of the great vessels with mild pulmonic stenosis, probably subvalvular.

*Edited by
Robert R. Montgomery, M.D.*

**All of these mammals, except one,
can synthesize vitamin C**



Woman (man) cannot.

Human beings can neither synthesize vitamin C nor store most of the water soluble vitamins. They should be replenished continuously.

Normally, people accomplish this in their daily diet. But under conditions of illness, stress, in convalescence or following surgery, vitamin stores may be depleted or metabolic demands increased.

In such cases, Surbex-T may be indicated. Surbex-T makes it easy and convenient to restore the water-soluble vitamins. Each tablet provides 500 mg. of vitamin C plus high potency B-complex.

Where nutritional status must be preserved, Surbex-T can help restore what the body *cannot* effectively store.

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SURBEX-T[®] 500 mg. of Vitamin C with High Potency B-Complex
Restores what the body cannot effectively store



The Antacid Analogy



Indications: Pro-Banthine is effective as adjunctive therapy in the treatment of peptic ulcer. Dosage must be adjusted to the individual.

Contraindications: Glaucoma, obstructive disease of the gastrointestinal tract, obstructive uropathy, intestinal atony, toxic megacolon, hiatal hernia associated with reflux esophagitis, or unstable cardiovascular adjustment in acute hemorrhage.

Warnings: Patients with severe cardiac disease should be given this medication with caution.

Fever and possibly heat stroke may occur due to anhidrosis.

In theory a curare-like action may occur, with loss of voluntary muscle

control. For such patients prompt and continuing artificial respiration should be applied until the drug effect has been exhausted.

Diarrhea in an ileostomy patient may indicate obstruction, and this possibility should be considered before administering Pro-Banthine.

Precautions: Since varying degrees of urinary hesitancy may be evident in elderly males with prostatic hypertrophy, such patients should be advised to micturate at the time of taking the medication.

Overdosage should be avoided in patients severely ill with ulcerative colitis.

Adverse Reactions: Varying degrees of drying of salivary secretions may

Therapeutic comparisons in peptic ulcer.

Antacids have only one mode of action to relieve ulcer pain...

Pro-Banthine[®] has four. and of propantheline bromide

Antacids:

Antacids relieve ulcer pain by neutralizing gastric acid. This action is relatively short-lived and they have no other mode of action.

Pro-Banthine:

Pro-Banthine suppresses gastric acid secretion. The antisecretory properties of Pro-Banthine are well established. By effectively blocking vagotonic impulses Pro-Banthine suppresses gastric secretion to reduce both total and free acid.

Pro-Banthine helps relieve pain.

Pro-Banthine relieves ulcer pain by reducing gastric secretion and the motility and spasm of the gastrointestinal tract.

Pro-Banthine reduces acidity without subsequent acid rebound. The capacity of Pro-Banthine to reduce the secretion of total and free acid in the stomach has been demonstrated in scores of studies. None has demonstrated any significant evidence of acid rebound.

Pro-Banthine activity lasts about six hours. The effect of a single therapeutic dose (15 mg.) of Pro-Banthine lasts about six hours.* Pro-Banthine P.A.[®], the prolonged-acting form, is active from 8 to 12 hours. Thus Pro-Banthine may be used to suppress acid, spasm, and pain around the clock, even during the sleeping hours when antacids, to be effective, must be taken almost hourly.

*Innes, I. R., and Nickerson, M., in Goodman, L. S., and Gilman, A. (editors): The Pharmacological Basis of Therapeutics, ed. 4, New York, The Macmillan Company, 1970, p. 537.

Pro-Banthine complements and enhances the action of antacids.

SEARLE

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San Juan, Puerto Rico 00936

Address medical inquiries to: G. D. Searle & Co.
Medical Department, Box 5110, Chicago, Ill. 60680

cur as well as mydriasis and blurred vision. In addition the following adverse reactions have been reported: nervousness, drowsiness, dizziness, insomnia, headache, loss of the sense of taste, nausea, vomiting, constipation, impotence and allergic dermatitis.

Dosage and Administration: The recommended daily dosage for adult ulcer therapy is one 15-mg. tablet with meals and two at bedtime. Subsequent adjustment to the patient's requirements and tolerance must be made.

Pro-Banthine P.A.—Each tablet of Pro-Banthine P.A. (propantheline bromide) contains 30 mg. of the drug in the form of sustained-release or

timed-release beads; on ingestion about half of the drug is released within an hour and the remainder continuously as earlier increments are metabolized. Thus the result is even, high-level anticholinergic activity maintained all day and all night in most patients with only two tablets daily. Some patients may require one tablet every eight hours.

The contraindications and precautions applicable to Pro-Banthine 15 mg. should be observed.

How Supplied: Pro-Banthine is supplied as tablets of 15 and 7.5 mg., as prolonged-acting tablets of 30 mg. and, for parenteral use, as serum-type vials of 30 mg.

Synthroid[®]

(sodium levothyroxine)



Supplied: **Tablets:** 0.025 mg., 0.05 mg., 0.1 mg., 0.15 mg., 0.2 mg., 0.3 mg., 0.5 mg., scored and color-coded in bottles of 100, 500, and 1000.

Injection: 500 mcg. lyophilized active ingredient and 10 mg. of Mannitol, U.S.P., in 10 ml. single-dose vial, with 5 ml. vial of Sodium Chloride Injection, U.S.P., as a diluent.

Synthroid-T₄



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The Rx that says "Relax"



BUTISOL Sodium provides highly predictable sedative effect: minor dosage adjustments are usually all that's needed to produce the desired degree of sedation. (With 3 dosage forms and 4 strengths to make adjustments easy.)

BUTISOL Sodium offers prompt, smooth, relatively non-cumulative action: begins to work within 30 minutes...yet, because of its intermediate rate of metabolism, generally has neither a "roller-coaster" nor a "hangover" effect.

BUTISOL Sodium is remarkably well tolerated: a 30-year safety record assures you that there is little likelihood of unexpected reactions.

BUTISOL Sodium saves your patients money: costs less than half as much as most commonly prescribed sedative tranquilizers.*

These are four good reasons for prescribing BUTISOL Sodium for the many patients who need to have the pace set just a little slower. Its gentle daytime sedative action is often all that's needed to help the usually well-adjusted patient cope with temporary stress.

*Based on surveys of average daily prescription costs.

Butisol  **SODIUM**
(SODIUM BUTABARBITAL)

Contraindications: Sensitivity or idiosyncrasy to barbiturates; history of manifest or latent porphyria or marked liver impairment; respiratory disease with dyspnea or obstruction; history of addiction to sedative/hypnotic drugs; uncontrolled pain, to avoid because of possible excitement.

Precautions: Exercise caution in: moderate to severe hepatic disease; anticoagulant therapy, because of possible increased metabolism of coumarin anticoagulants; withdrawal in drug dependence or the taking of excessive doses over a long period, to avoid withdrawal symptoms; elderly or debilitated patients, to avoid possible marked excitement or depression; use with alcohol or other CNS depressants, because of combined effects.

Adverse Reactions: Slight hangover, drowsiness, lethargy, headache, skin eruptions, nausea and vomiting, hypersensitivity reactions (especially in those with asthma, urticaria, angioneurotic edema, or similar conditions).

Usual Adult Dosage: For daytime sedation, 15 mg. to 30 mg. t.i.d. or q.i.d. For hypnosis, 50 mg. to 100 mg.

Available as: Tablets, 15 mg., 30 mg., 50 mg., 100 mg.; Elixir, 30 mg. per 5 cc. (alcohol 7%). BUTICAPS® [Capsules BUTISOL SODIUM (sodium butabarbital)] 15 mg., 30 mg., 50 mg., 100 mg.

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acute gonorrhea

This patient
just received
an effective, private,
physician-controlled
treatment.

It took just one short visit.



*Urethritis, cervicitis, proctitis when due
to susceptible strains of *N. gonorrhoeae*

Trobicin—The advantage of injectable therapy.

Once Trobicin is injected, treatment is usually complete; there can be no problems with patients sharing, skimping, skipping or forgetting medication.

Trobicin—The aspect of privacy.

There are no prescriptions to fill, no capsules to take. Neither family, friends nor co-workers need know or suspect the patient's problem.

Trobicin—Indication and dosage.

Spectinomycin is indicated only for use in acute urethritis and proctitis in the male and acute cervicitis and/or proctitis in the female when due to susceptible strains of *N. gonorrhoeae*. The usual dosage for Trobicin in adult males is 2 grams intramuscularly†; 4 grams intramuscularly in females.

Trobicin—Not effective for syphilis.

Trobicin is not effective for any stage of syphilis. Trobicin may mask or delay the symptoms of incubating syphilis. If concurrent syphilis is suspected, follow the patient serologically for at least 3 months. Patients with syphilis should receive adequate specific anti-syphilitic therapy with an appropriate antibiotic.

Trobicin is contraindicated in patients previously found hypersensitive to it.

Intramuscular

...and **Trobicin**® 2 gm and 4 gm vials sterile spectinomycin hydrochloride

Sterile Trobicin

Sterile Trobicin (spectinomycin hydrochloride)
—For Intramuscular Injection:

2 gm vials containing 5 ml when reconstituted with diluent.

4 gm vials containing 10 ml when reconstituted with diluent.

An aminocyclitol antibiotic active *in vitro* against most strains of *Neisseria gonorrhoeae* (MIC 7.5 to 20 mcg/ml). Definitive *in vitro* studies have shown no cross resistance of *N. gonorrhoeae* between spectinomycin and penicillin.

Indications: Acute gonorrheal urethritis and proctitis in the male and acute gonorrheal cervicitis and proctitis in the female when due to susceptible strains of *N. gonorrhoeae*.

Contraindications: Contraindicated in patients previously found hypersensitive to spectinomycin.

Warnings: Not indicated for the treatment of syphilis. Antibiotics used to treat gonorrhea may mask or delay the symptoms of incubating syphilis. Patients should be carefully examined and monthly serological follow-up for at least 3 months should be instituted if the diagnosis of

syphilis is suspected.

Safety for use in infants, children and pregnant women has not been established.

Precautions: The usual precautions should be observed with atopic individuals. Clinical effectiveness should be monitored to detect evidence of development of resistance by *N. gonorrhoeae*.

Adverse reactions: The following reactions were observed during the single-dose clinical trials: soreness at the injection site, urticaria, dizziness, nausea, chills, fever and insomnia. During multiple-dose subchronic tolerance studies in normal human volunteers, the following were noted: a decrease in hemoglobin, hematocrit and creatinine clearance; elevation of alkaline phosphatase, BUN and SGPT. In single- and multiple-dose studies in normal volunteers, a reduction in urine output was noted. Extensive renal function studies demonstrated no consistent changes indicative of renal toxicity.

Dosage and administration: Keep at 25° C and use within 24 hours after reconstitution with diluent.

Male—Inject 5 ml intramuscularly for a 2 gram dose. Patients with gonorrheal proctitis and patients being re-treated after failure of previous antibiotic therapy should receive 4 grams (10 ml). In geographic areas where antibiotic resistance is known to be prevalent, initial treatment with 4 grams (10 ml) intramuscularly is preferred.

Female—Inject 10 ml intramuscularly for a 4 gram dose.

How supplied: Vials, 2 and 4 grams—with ampoule of Bacteriostatic Water for Injection with Benzyl Alcohol 0.9% w/v. Reconstitution yields 5 and 10 ml respectively with a concentration of 400 mg spectinomycin per ml (as the hydrochloride). For intramuscular use only. **Susceptibility Powder**—for testing *in vitro* susceptibility of *N. gonorrhoeae*.

Caution: Federal law prohibits dispensing without prescription.

For additional product information see your Upjohn representative or consult the package insert.

Upjohn

The Upjohn Company, Kalamazoo, Michigan 49001

MED B-5-S (MBR-1)

†For patients with gonorrheal proctitis and for patients in geographic areas where antibiotic resistance is known to be prevalent, initial treatment with 4 grams is preferred.

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In East Harlem, the AMA helped a lot of addicts kick it.

"Where can I get help? What will happen to me? Will I be arrested? Who can I trust? For an addict, the answers are often critical to his decision to seek help.

In East Harlem, he knows where he can get the right answer and help: the Drug Referral Agency right in his community. It's staffed by former addicts who are intimately familiar with an addict's needs. Since opening its door, the agency has helped hundreds of addicts kick the habit.

This referral service was part of a pilot demonstration project initiated by the East Harlem Community with the help of the Mt. Sinai School of Medicine and the AMA.

Why did the AMA get involved? To help develop a model other communities can use as a guide in developing their own drug abuse programs.

Physicians often wonder what the AMA really does. This is one of many things — all made possible by the physicians who support the AMA through their membership. Find out more about the AMA. Just send in the completed coupon.

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Entrapped gas...

Silent partner of GI spasm

Painful GI spasm in the presence of entrapped gas causes even more pain and more discomfort. Yet, while spasm is relieved, entrapped gas often goes untreated.

Not so when you prescribe Sidonna. Sidonna helps release entrapped gas with specially activated simethicone, a nonsystemic antifoaming agent, while also helping to relieve spasm with a traditional combination of belladonna alkaloids. And Sidonna provides mild sedation with butabarbital.

Sidonna. The therapeutic partnership approach to functional or organic GI disturbances including spastic colon, irritable bowel syndrome, gastroenteritis, gastritis, peptic ulcer and nervous indigestion.

Contraindications: hypersensitivity to barbiturates or belladonna alkaloids; glaucoma, prostatic hypertrophy, pyloric obstruction. **Side Effects:** dry mouth, blurred vision, dysuria, skin rash, constipation or drowsiness. **Dosage:** one or two tablets preferably before meals and at bedtime.

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Sidonna®

Each scored tablet contains: specially activated simethicone 25 mg., hyoscyamine sulfate 0.1037 mg., atropine sulfate 0.0194 mg., hyoscine hydrobromide 0.0065 mg. (equivalent to belladonna alkaloids [as bases] 0.1049 mg.) and butabarbital sodium N.F. 16 mg. (Warning: may be habit forming.)

**A working partnership
against the
pain of gas and spasm**

What's on your patient's face...

may be more important than his chief complaint

Patient P.T.* seen on 3/29/67 shows typical lesions of moderately severe keratoses. Note residual scarring on ridge of nose from previous cryosurgical and electrosurgical procedures.



Patient P.T.* seen on 6/12/67, seven weeks after discontinuation of 5% FU cream. Reaction has subsided. Residual scarring not seen except that due to prior surgery. Inflammation has cleared and face is clear of keratotic lesions.

*Data on file,
Hoffmann-La Roche
Inc., Nutley, N.J



The lesions on his face are solar/actinic— so-called "senile" keratoses... and they may be premalignant.

Solar, actinic or senile keratoses

These lesions may be called by several names, but they usually can be identified by the following characteristics. The typical lesion is flat or slightly elevated, of a brownish or reddish color, papular, dry, rough, adherent and sharply defined. They commonly occur as multiple lesions, chiefly on the exposed portions of the skin.

Sequence of therapy— selectivity of response

After several days of therapy with Efudex® (fluorouracil), erythema may begin to appear in the area of the lesions; this reaction usually reaches its height of unsightliness and discomfort within two weeks, declining after discontinuation of therapy. This reaction occurs in affected areas. Since the response is so predictable, lesions that do not respond should be biopsied.

Acceptable results

Treatment with Efudex provides highly favorable cosmetic results. Incidence of scarring is low. This is particularly important with multiple facial lesions. Efudex should be applied with care near the eyes, nose and mouth.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Multiple actinic or solar keratoses.

Contraindications: Patients with known hypersensitivity to any of its components.

Warnings: If occlusive dressing used, may increase inflammatory reactions in adjacent normal skin. Avoid prolonged exposure to ultraviolet rays. Safe use in pregnancy not established.

Precautions: If applied with fingers, wash hands immediately. Apply with care near eyes, nose and mouth. Lesions failing to respond or recurring should be biopsied.

Adverse Reactions: Local—pain, pruritus, hyperpigmentation and burning at application site most frequent; also dermatitis, scarring, soreness and tenderness. Also reported—insomnia, stomatitis, suppuration, scaling, swelling, irritability, medicinal taste, photosensitivity, lacrimation, leukocytosis, thrombocytopenia, toxic granulation and eosinophilia.

Dosage and Administration: Apply sufficient quantity to cover lesion twice daily with nonmetal applicator or suitable glove. Usual duration of therapy is 2 to 4 weeks.

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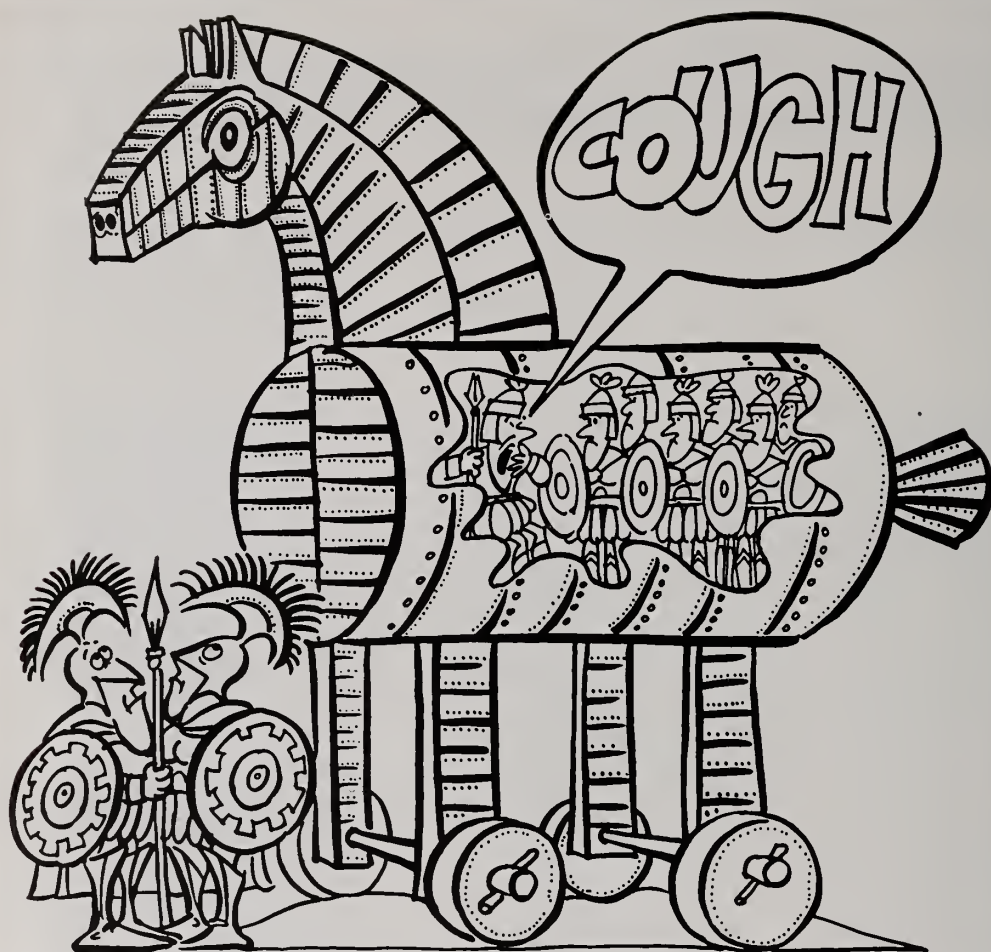
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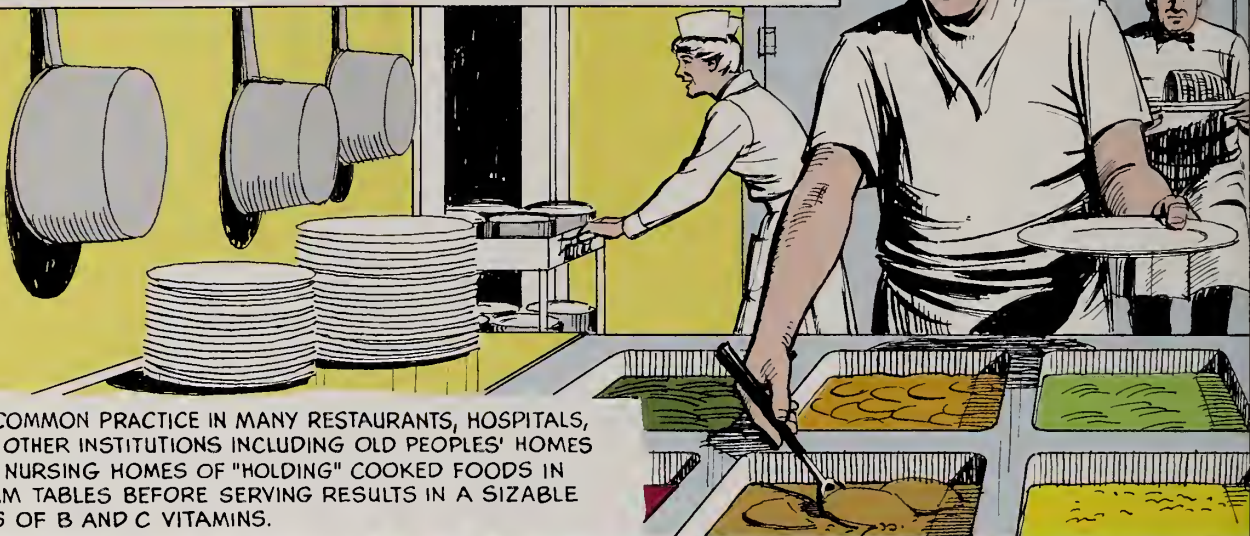
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atropine sulfate	0.0194 mg.	0.0194 mg.	0.0582 mg.
hyoscine hydrobromide	0.0065 mg.	0.0065 mg.	0.0195 mg.
phenobarbital	($\frac{1}{4}$ gr.) 16.2 mg.	($\frac{1}{2}$ gr.) 32.4 mg.	($\frac{3}{4}$ gr.) 48.6 mg.
(warning: may be habit forming)			

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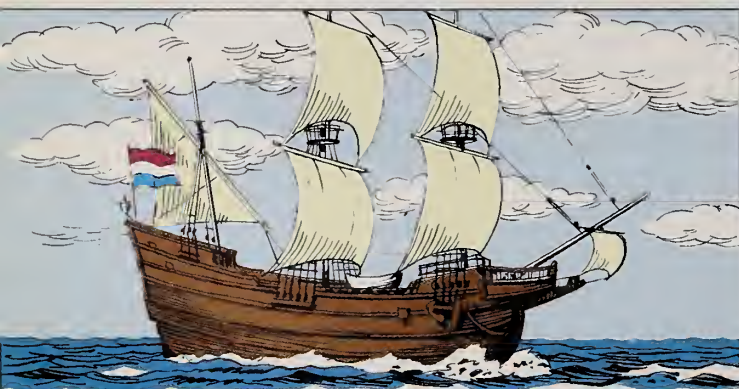
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BOOK REVIEWS

Clinical Aspects of Thromboembolism. W. R. PITNEY, M.D., FRACP, FRCPA. Price, \$15.75. Pp. 194. Baltimore, Maryland: The Williams and Wilkins Company, 1972

The author located at the school of medicine, St. George Hospital, Kagarah 227, N.S.W., states this is intended as a practical guide to diagnosis and management of patients with **THROMBOEMBOLISM**. Chap. 1 mechanisms of thrombosis, indicates that often there are multiple factors in thrombosis; while predisposing causes may be evident, the nature of the triggering mechanism is often not evident. Other Chapters, No. 2, discusses deep vein thrombosis; Ch. 3, diagnosis of venous and pulmonary embolism; 4, prevention of thrombosis; 5, on oral anticoagulants; 6, on heparin; 7, on therapeutic defibrination; 8, thrombolytic therapy and 9, guidelines to management.

Heparin, ancrod and the oral anticoagulants prevent the formation or propagation of thrombi, but possess no significant lytic effect on pre-existing thrombi. Also discussed in some detail are the agents **STREPTOKINASE AND UROKINASE**; both act by producing intense fibrinolytic activity in the blood during the period of administration. Many factors, in the illness of a patient with thrombolytic phenomena, may modify the choice of a therapeutic agent. Whether to treat the patient actively, the duration of treatment, as well as the surgical treatment of the patient, are discussed where pertinent. Other topics covered are: prophylaxis of venothrombosis, types of thrombophlebitis, venous thrombosis in pregnancy, single massive pulmonary embolism, recurrent pulmonary embolism, etc. In myocardial infarction several approaches to its treatment by anticoagulants are considered. In cerebral vascular disease, there is no place for anticoagulant or thrombolytic therapy in established strokes due to cerebral thrombosis. Finally anticoagulant in intravascular coagulation is given.

Recommendation: This book is intended as a guide to physicians and nurses involved in the care of patients with **THROMBOEMBOLISM**. It gives a good resumé of the various agents used in common clinical situations. A unique feature of this monograph are the many references from the pertinent literature on the subject under consideration; for example, Chap. 2 has 90 and Chap. 8 has 58 references to the pertinent literature. This monograph is best used as a reference work for physicians and nurses engaged in emergency care, diagnosis and treatment of patients with thromboembolism and its associated phenomena. **BENNIE A. MOXNESS, M.A., M.D.**

Rise Up To Life. LEONARD BICKEL. Price, \$9.95. Pp. 314 with illustrations. New York: Charles Scribner's Sons, 1972.

In this biography of Howard Walter Florey, according to author Bikel, Florey was a man possessing great courage, imagination and judgment, who was continuously working under pressures while carrying out his scientific research in the development of penicillin. He felt keenly the lack of financial support and assistance in his program and it was not until late in the study that he received substantial funds from the Medical Research Council and the Rockefeller Foundation (now University). In spite of clinical successes in the treatment of sepsis and septicaemia, especially through application of penicillin by Ethel Florey, he did not gain the full support of practicing physicians and surgeons, who showed resistance to its use because of their relying on the use of sulfonamides in combatting infection. It was through his tenacity of purpose as well as his faith in his ideas that Florey succeeded. No doubt Fleming overshadowed Florey, but the latter was more responsible and indeed contributed towards the final acceptance and use of penicillin in the treatment of many types of infections and venereal diseases.

Florey began his scientific investigation on Lysozyme but in 1938 he commenced his studies with penicillin. He believed in a joint study program including multidiscipline basic medical sciences such as biochemistry, bacteriology and the biological aspects (pathology and physiology).

There were technical difficulties, which plagued his early endeavors in obtaining adequate yield of penicillin. Subsequently, two events happened. First, his co-worker Headley developed a method, "a back extraction from ether into a neutral buffer," increasing the yield of penicillin from the substance in the filtrate of mould juice substrate or mould broth. Secondly, later through the growth of mould in American "corn steep liquor" with its sugar nutrient caused a jump in the penicillin yield. This came about through Doctor R. Coghill of Peoria, Ill., and following this, penicillin became available for clinical application. Those physicians who practiced during the early 1940's can remember how costly penicillin was and the difficulties in obtaining small quantities of penicillin. Because of the limited supply, penicillin was allotted and apportioned to the military and later distributed to civilian practice.

Many names appear in connection with the development of penicillin as a weapon against common sepsis. A partial list is presented.

BOOK REVIEWS

- 1928 Sir Alexander Fleming discovered the mould penicillin naming it penicillin notatum.
- 1941 Dr. Shelman Waksman coined antibiotic to denote chemotherapeutic substances basically produced by natural processes.
- 1940 Co-workers Ernst-Chain, Dr. Norman Headley and Dr. Margaret Jennings were members of the team besides others at Oxford. They decided the standard measure denoting the activity of penicillin. This was the "Oxford Unit" and was adopted later as the international standard.
- 1940 Dr. Martin Dawson at Presbyterian Hospital, New York, gave the first injection of penicillin in treating a patient.
- 1941 During Florey's visit to the United States he met Professor Ross Harrison, President of the National Academy and Dr. John Fulton whom he knew, as both Fulton and Florey were Rhodes Scholars. He met Dr. Rene Dubois, who in turn introduced him to the American followers of his penicillin therapy. Also, he met Dr. A. N. Richards who was instrumental in getting the support of the leaders of the United States drug industry and as a result, Florey was able to get penicillin on a much larger scale.
- 1942 Major R. Pulverstaff administered the first penicillin in the War Zone at the 15th Scottish General Hospital, Cairo.
- 1942 Lieutenant-Colonel Rudolph Schullinger was a pioneer in using penicillin for clinical trial in Military Surgery.
- 1944 The United States Army adopted penicillin as the routine treatment of syphilis.

Dr. Howard Florey received many awards including the Nobel Prize in 1945, the Lomonoss Medal, Associate membership in the Soviet Academy, the Royal Danish Academy of Sciences, the American Philosophical Society, Chancellor of the Australian National University, raised to peerage in 1965 and many other honors.

His first professional chair was the post of Joseph Hunter Professor of Pathology at University of Sheffield. His last major achievement was the presidency of the Royal Society.

This account of the Life of Florey is a remarkable story and portrays the struggles and obstacles-technical difficulties and personality conflicts and differences met and surmounted through his perseverance. A new era in medicine followed with the advent and use of penicillin.

The author's style is easy and entertaining reading and incorporates Florey's association with and correspondence between him and many great men of science and medicine such as Sir Charles Sherrington, Ramon Y Cajal and Sent-Gyorgyi and others.

Baron Howard Walter Florey, of Adelaide, in the Commonwealth of Australia and Marston, in the County of Oxford, died in February 1968 at age 70 years.

JOHN G. STUBENBORD, M.D.

Handbook of Ocular Therapeutics and Pharmacology. PHILIP P. ELLIS, M.D. AND DONALD SMITH, M.D., Ph.D. Price, \$14.75. Pp. 262. St. Louis: C. B. Mosby Company, 1973.

This book was written to serve as a quick reference for the busy practicing ophthalmologist, as a guide in therapy for beginning residents in ophthalmology, and for non-specialists who are treating ocular disorders. It presents in a concise form the basic considerations of current ocular therapy and pharmacology with emphasis on the most significant practical and effective forms of current therapy.

The handbook is divided into two sections. The first section on therapeutics discusses some basic considerations on the mechanism by which drugs act on the eye, how they are prepared, and the principles of cortisone and antibiotic therapy followed by chapters on the therapy of diseases affecting various parts of the eye and orbit. The second section lists all of the drugs referred to the first section in alphabetical order, discusses in adequate detail their mechanisms of action, side reactions, and contraindications, and the preparations and dosage forms available and recommended.

This arrangement does result in a fair amount of repetition of material. An excellent four-page table on chemotherapeutic and antibiotic agents is duplicated in both sections. It might have been more efficient to combine both sections and depend entirely on the index for quick referral to the particular information desired.

A useful table at the end of the book is one on standard pediatric dosages which emphasizes the

importance of weight and size in drug usage.

The author states that the incidence of iritis after echothiophate iodine therapy may be greatly reduced by using 2.5% phenylephrine (Neo-Synephrine) as the dilutant. Because of the stability problems involved, it would be best to use the two medications separately. One wonders if it is desirable to have detailed information on treatments of certain ocular conditions which are usually best handled by the non-ophthalmologist, such as anti-coagulant therapy for arterial and venous thrombosis of the retinal vasculature and chemotherapy for the treatment of ocular tumors such as retinoblastoma or malignant melanoma. In addition, the therapy of eyelid lesions due to either systemic or discoid lupus erythematosus, syphilis, tuberculosis and leprosy are rather amply discussed. It is informative but the ophthalmologist should only treat these conditions if no other medical consultation is available. The beneficial use of newer modalities of therapy such as the soft hydrophilic contact lens, and tear substitutes such as Adsorboteers are adequately presented.

The authors state that one of the side effects of topical steroid therapy is ocular hypertension or glaucoma. This rise in intraocular pressure occurs in about 30% of all patients after 2-4 weeks of treatment. However, if this book is going to be of real benefit to the non-ophthalmologist who frequently uses topical steroids in the treatment of allergic conjunctivitis, he would be best advised to always tell the patient to get his intraocular pressure taken if he provides enough medication to last more than 3 weeks. Serious loss of vision has occurred even in relatively young individuals.

The authors have succeeded in providing a quick reference source containing much useful information on therapy and drugs.

HOWARD N. BERNSTEIN, M.D.

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Lyons, W.S., Peabody, J.W.: Complications of Cardiac Pacemakers, Medical Annals of D.C., 1973, 42, 165.

TEXT

Use generic or descriptive names of drugs when available. Trade names, capitalized, may be given in parentheses when the drug is first mentioned.

Statistics should be checked for consistency within the text and for agreement with graphs or tables.

Laboratory data should not be given in abbreviated form but in full (e.g., "hemoglobin level, 12 Gm. per 100 ml." rather than "Hb. 12 GM.%").

Figures should be used for number 10 and above, laboratory measurements, percentages, and ages.

Metric equivalents should be given for dosage and body height and weight.

Centigrade equivalents should be given for Fahrenheit body temperatures, and vice versa.

Abbreviations should be used sparingly, with expansion given for those not listed in standard medical dictionaries.

The meaning of "we" should be clarified, especially if there is only one author. Avoid use of editorial "we."

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INDEX TO ADVERTISERS

Equipment and Supplies			
Kloman Surgical Supply Company	2	Dorsey Laboratories	T-274
Insurance		Flint Laboratories	T-266
Corroon & Black, Russell, Inc	6	Eli Lilly & Company	14
Ralph W Lee & Company	T-284	McNeil Laboratories	T-267
Mutual of Omaha	4	Pharmaceutical Manufacturers Association	12-13
Nurse Registries		Reed & Carnrick	T-271
District of Columbia Manpower Administration	T-284	A. H. Robins Company	T275, 276
Nutrition Education		Roche Laboratories	c2, 1, 10-11, T-272-273, c4, c4
Dairy Council of Greater Metropolitan Washington, D.C.	2	G. D Searle & Company	T264-265
Pharmaceuticals		The Upjohn Company	T268-269
Abbot Laboratories	T-263	Pharmacy	
Burroughs Wellcome & Company	9	Peoples Drug Stores	T-278
		Therapy	
		The University Center	6

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Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

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For further information on this subject, the following references are provided:

1. Henry BW, *et al*: *Dis Nerv Syst* 30:675-679, Oct 1969.
2. Hollister LE, *et al*: *Arch Gen Psychiatry* 24:273-278, Mar 1971.
3. Claghorn J: *Psychosomatics* 11:438-441, Sept-Oct 1970.



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surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of child-bearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies.

Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle

spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.



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CONTENTS

SCIENTIFIC ARTICLES

Primary Hyperparathyroidism. Luis A. Mispireta, M.D., Noel M. Doromal, M.D. and Mario H. Diaz, M.D.	285
Mesenteric Vascular Disease: Clinical Features and Review of the Literature. Alberto J. Muniaguirria, M.D. and Allender Sybert, M.D.	295
Surgical (and Medical) Sequelae of Drug Addiction. Glenn W. Geelhoed, M.D.	307

SPECIAL ARTICLE

PSRO, SSA and Private Practice of Medicine. Russell D. Squires, M.D. and Paul R. Moyer, M.D.	317
--	-----

OTHER FEATURES

President's Message	5
Acupuncture. Clifton Gruver, M.D.	7
Scientific Editorial	7
Anticoagulation IV: Preventing Thrombosis by Modifying Platelet Behavior. Edward Adelson and Amiel Segal.	294
The View Box	294
Edited by Gunther J. Augustin, M.D.	306
ECG Problems	306
Edited by Robert R. Montgomery, M.D.	337
Information for Authors	340
Advertising and Subscription Information	340
Index to Advertisers	340

This issue of the **MEDICAL ANNALS OF THE DISTRICT OF COLUMBIA** is devoted to the first, second and third place winners of the **Dr. Philip Burka Award and Citation**. The awards were presented **April 10** at the Annual Dinner Meeting of the Medical Society. The Awards were established in 1969 by the Burka family and sponsored by the Medical Society of D.C. The three scientific papers appear in the award winning order.

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PRESIDENT'S MESSAGE

ACUPUNCTURE

The deliberations of the City Council and its decisions relative to the practice of Acupuncture (on the basis of public hearings May 28 and 30) may be history by the time this editorial reaches print. Nevertheless, it seems appropriate to reiterate the Medical Society's position and review the chain of events since Acupuncture has come to our town.

In the fall of 1972, the Commission on Licensure for the District of Columbia responded to an inquiry by a New York physician that its interpretation of our statutes in the Healing Arts Act permitted Acupuncture treatment by, or under the direct supervision of, any duly licensed and qualified physician. (It also indicated that such a physician possess the training and skills to responsibly supervise the act). This opened the floodgates for the influx of the Acupuncture clinics into this capital city of our nation.

The burgeoning of Acupuncture clinics has brought with it a flavor of the occult and the mystic, oriental symbols and terms such as the "yin and the yang" and "chi." It also raised the hopes of the poor, downtrodden sufferers of chronic disorders incurable by Western medicine standards. Ripe for the pluckin', it led to the "bussing" in of such victims to these clinics from other areas of the East Coast or, from more widespread geographical locales. It led to ethical deteriorations of unbelievable proportions. Flagrant commercialism and solicitation of patients has been seen in large newspaper ads, TV spots, even classified ads in distant cities. All of this solicitation led in the direction of the Washington mecca. It also raised the spectre of owners of shady character, who had found abortions no longer good business.

With the advent of Acupuncture to our city, the Medical Society promptly created an Ad Hoc Committee for its study, and to recommend guidelines. This resulted in a policy statement on Acupuncture which the Society issued on March 26, 1973, and reaffirmed on October 29, 1973. The Ad Hoc Committee has again reviewed and maintains that position in this month of May, 1974. It should be emphasized that the Society is not opposed to the concept of Acupuncture per se. Its initial remark in that statement "recognizes the need for and desires to encourage further research in the techniques, mechanism of action, and uses of acupuncture. However, because acupuncture is considered at this time strictly an investigational procedure, it should be performed only in medical centers and teaching hospitals having committees on human research, which shall be subject to the necessary peer review of protocols and appropriate monitoring by the Medical Society of the District of Columbia's peer review and utilization mechanisms." It goes on to state "because of the lack of understanding by Western medical scientists and because of potential harm which acupuncture might produce in patients for whom the treatment of symptoms would mask a serious or perhaps fatal condition otherwise amenable to treatment aimed at its cause, the Medical Society of the District of Columbia has concluded that, at this time, acupuncture is not sufficiently understood to be accepted without constraints for use in the practice of medicine in the District of Columbia."

This posture has been repeatedly stated to the Commission, to our membership, and to the public via the news media. We have expressed our concern vociferously over the presence of "therapists" for whom we have no definition, no method for determination of qualifications or certification (as for any other practitioner in the Healing Arts), indeed, no ability to even communicate, for the most part.

These acupuncturists are practicing in our city, upon our citizens. To conform to the "letter" of the law, they are under the "supervision" of Western physicians who have little or no understanding or experience with Acupuncture. We have concern that even their preliminary physical exams are inadequate for the appropriate diagnosis of the ailment, and that their medical records leave much to be desired.

Certainly, this does not conform to the "intent" of the law as the Commission on Licensure interpreted it.

Furthermore, we do not believe that the clinic treatments are as innocuous as the public might be led to believe ("at least no harm is done" appears in one brochure). Over and above the public health hazard of "masking" a disorder, we are aware of overt complications of infection, bleeding and ecchymoses, foreign bodies left in the tissues (needles), burns from moxibustion, pneumohemothorax, etc.

Acupuncture, as a treatment modality used for analgesia or in anesthesia, is being researched and may yet prove to be a useful adjunct to our therapeutic armamentarium. Its use in the healing arts as for neurologic diseases (multiple sclerosis, etc.) and nerve deafness—as has been widely proclaimed—is not just questionable, but has been discredited through such studies as "Acupuncture for Hearing Loss," Fairbanks, Wallenberg, and Webb from the Otolaryngology Section of the Medical Society of the District of Columbia—to be published in the next issue of these ANNALS. The victimization of patients, the unwarranted raising of their hopes, and the financial sacrifices involved for many are all tragic.

The Medical Society intends to make these points loud and clear at the upcoming hearings. We hope and pray that uninformed public clamor and the wiles of the clinics do not obstruct achieving the constraints necessary to protect the public health of our community.

Although it may now be after the fact, I want to reiterate the Society's stand on Acupuncture for the membership, and the reasons leading to that posture.

CLIFTON R. GRUVER, M.D.
PRESIDENT



Clif Gruver

DR. CLIFTON GRUVER

SCIENTIFIC Editorial

ANTICOAGULATION IV: PREVENTING THROMBOSIS BY MODIFYING PLATELET BEHAVIOR

Edward Adelson and Amiel Segal

The importance of preventing arterial and venous clots is evident from the incidence of mortality from coronary thrombosis, cerebral thrombosis and embolism, and pulmonary embolism. Heparin and coumarin have been widely used because they inhibit the coagulation cascade and thereby retard fibrin clot formation. Arterial thrombi, however, begin as masses of platelets. Fibrin is laid down only in the tail of the thrombus as it ages. Such arterial or platelet thrombi might best be prevented, therefore, by agents that modify platelet behavior. Theoretically, even venous thrombi might be prevented by antiplatelet agents, for some data suggest that these venous clots may also begin as small platelet plugs.

The anti-inflammatory drugs—aspirin, indomethicin, chloroquine, phenylbutazone and sulfinpyrazone—have all been shown to modify platelet behavior. Vasoactive drugs, especially dipyridamole (Persantin^R) also alter platelet clumping. Antihistamines, such as cryptoheptadine (Periactin^R), have also been used for this purpose. And, dextran, either in the low-molecular weight (Rheomacrodex^R, Dextran-40^R), or in the middle-molecular weight range (Dextran-70^R) inhibit platelet function by coating the platelet. Hydroxyethyl starch, a newer volenic colloid, may have some use through a similar mechanism. Of these agents, aspirin and dipyridamole appear to be the most promising for clinical use.

Aspirin prevents the secondary release of ADP from platelets and inhibits the clumping of platelets induced by collagen. Altered platelet function may persist for days, even after a single aspirin tablet. Aspirin has been shown to decrease the size of experimentally induced myocardial infarcts in dogs.¹ There was a diminished incidence of myocardial infarction and cerebrovascular accidents in patients with rheumatoid arthritis on long-term aspirin therapy.² There was not a single case of coronary or cerebral thrombosis in 8,000 patients who received one or two aspirin tablets daily as a part of a long-term study.³ In one study,⁴ aspirin was as effective as warfarin in preventing venous

thromboembolism in patients undergoing hip arthroplasties, while in another study,⁵ warfarin was more effective than aspirin. It should be pointed out, however, that aspirin is not a completely benign drug. It causes gastritis and may produce a bleeding diathesis, especially in patients being simultaneously treated with coumarin. Furthermore, no long-term, well-controlled, double-blind studies have been carried out to determine the true value of aspirin therapy in the prevention of either arterial or venous thrombosis.

Dipyridamole inhibits the aggregation of platelets that is induced by ADP, and has had fairly extensive experimental and clinical trials. In doses of 100 milligrams 4 times per day, dipyridamole restored the shortened platelet survival toward normal in patients with prosthetic heart valves, plastic arteriovenous cannulas, arterial thromboembolism, hemolytic uremic syndrome, and thrombotic thrombocytopenic purpura.⁶ The same effect was accomplished by adding 1.2 grams of aspirin daily to a reduced dose of dipyridamole (100 milligrams per day). In another study,⁷ patients with prosthetic heart valves treated with warfarin had a 14.3 percent incidence of arterial thrombi; this was reduced to 1.3 percent when dipyridamole was added at a dose of 100 milligrams 4 times per day. As with aspirin, not all reports using dipyridamole are favorable,⁸ and we must await the results of well-controlled double-blind studies.

The clinical value of aspirin or dipyridamole has not yet been firmly established. Nevertheless, the physician caring for a patient with recurrent arterial thrombi is faced with a dilemma. He must first rule out diseases like subacute bacterial endocarditis, myxoma of the atrium, collagen vascular diseases, and the other diseases associated with vasculitis. Having done so, he will probably try the usual anticoagulants. However, if the disease persists in spite of therapy with heparin or coumarin, he will be faced with the decision of whether to add or to substitute aspirin or dipyridamole. If he uses aspirin, a reasonable dose would be 4 tablets per day (1.2 grams). If he uses dipyridamole, the dose should be

100 milligrams 4 times a day. If he elects to combine dipyridamole and aspirin, the dose of dipyridamole should be reduced to 100 milligrams per day. And, as was pointed out earlier, when aspirin is used in combination with coumarin, the patient must be watched closely because of the added risk of hemorrhage. For this reason, if the decision is made to combine aspirin with an anti-coagulant, it may be safer to use aspirin with heparin rather than coumarin.

References

1. MOSHOS, C. B., LAHIRI, K., LYONS, M., WEISSE, A. B., OLDEWURTEL, H. A., REGAN, T. J.: Relation of Microcirculatory Thrombosis to Thrombus in the Proximal Coronary Artery: Effect of Aspirin, Dipyridamole, and Thrombolysis. *Am. Heart J.* 1973, 86:61-8.
2. WOOD, L.: Treatment of Arteriosclerosis and Thrombosis with Aspirin. *Lancet* 1972, 2:532-3.
3. CRAVEN, L. I.: Prevention of Coronary and Cerebral Thrombosis. *Mississippi Valley Med. J.* 1956, 78:213.
4. SALZMAN, E. W., HARRIS, W. H., DE SANCTUS, R. W.: Reduction in Venous Thromboembolism by Agents Affecting Platelet Function. *New England J. Med.* 1971, 284:1287-92.
5. OBRIEN, J. R., TULEVAKI, V., ETHERINGTON, M.: Two *in vitro* studies comparing high and low aspirin dosage. *Lancet* 1:399-400.
6. HARKER, L. A., SLICHTER, S. J.: Platelet and Fibrinogen Consumption in Man. *New Eng. J. Med.* 1972, 287:999-1005.
7. SULLIVAN, J. M., HARKER, D. E., GORLEIN, R.: Pharmacologic Control of Thromboembolic Complications of Cardiac Valve Replacement. *New Eng. J. Med.*, 1971, 284:1391-4.
8. ACHESON, J., DANTE, G., HUTCHINSON, E. C.: Controlled Trial of Dipyridamole in Cerebral Vascular Disease. *Brit. Med. J.* 1969, 1:614-5.



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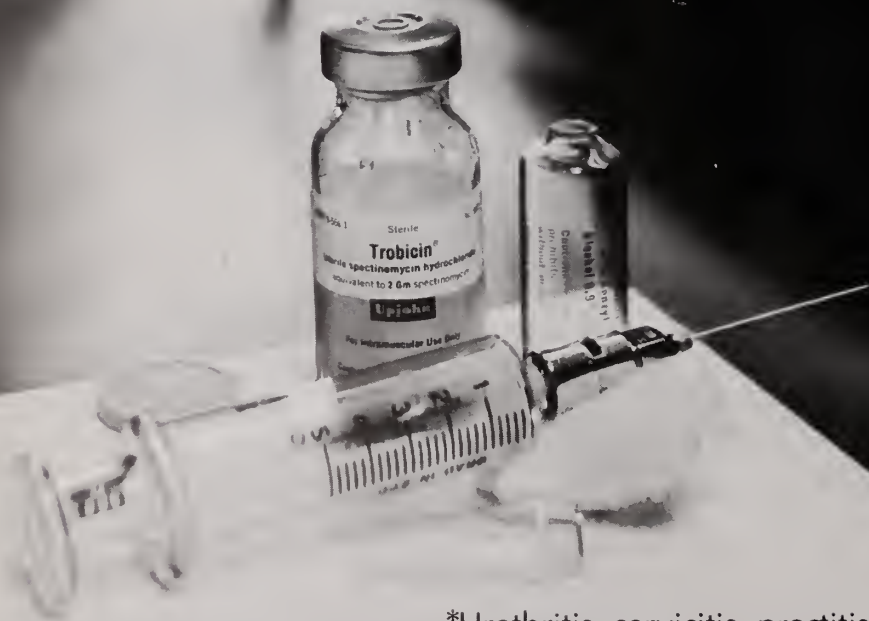
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Contraindications: Contraindicated in patients previously found hypersensitive to spectinomycin.

Warnings: Not indicated for the treatment of syphilis. Antibiotics used to treat gonorrhea may mask or delay the symptoms of incubating syphilis. Patients should be carefully examined and monthly serological follow-up for at least 3 months should be instituted if the diagnosis of

syphilis is suspected.

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Precautions: The usual precautions should be observed with atopic individuals. Clinical effectiveness should be monitored to detect evidence of development of resistance by *N. gonorrhoeae*.

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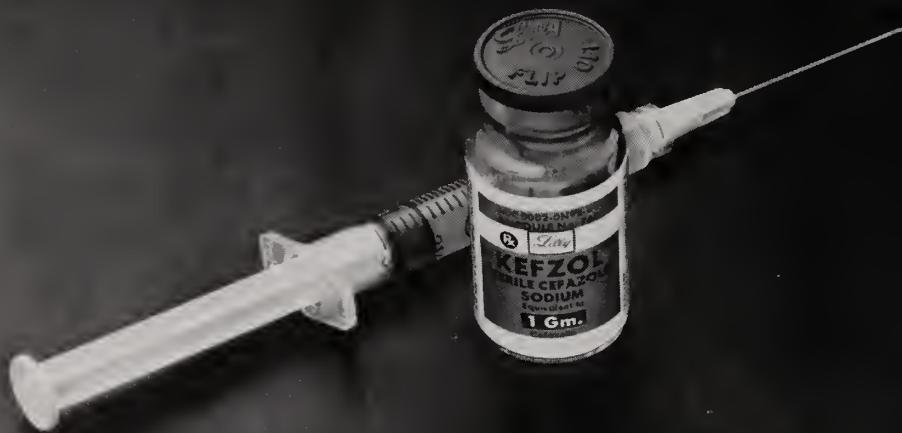
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SCIENTIFIC ARTICLES

Primary Hyperparathyroidism

LUIS A. MISPIRETA, M.D., NOEL M. DOROMAL, M.D. AND MARIO H. DIAZ, M.D.

Abstract

Thirty-three patients with primary hyperparathyroidism are presented. The following facts are stressed: (1) Patients with primary hyperparathyroidism have many nonspecific manifestations. The physician should have a high index of suspicion if he is to diagnose this condition before complications appear; (2) Persistent hypercalcemia remains the only readily available, accurate laboratory determination in the diagnosis of primary hyperparathyroidism; (3) The surgeon in a community hospital should be thoroughly familiar with the disease because of the lack of accurate laboratory methods available to localize the position of the abnormally functioning parathyroid gland; and (4) On the basis of this report we do not recommend a near total parathyroidectomy for the treatment of hyperparathyroidism except in patients with proven diffuse hyperplasia.

Introduction

Primary hyperparathyroidism may be due to one or more parathyroid adenomas, to hyperplasia of the parathyroid glands or to carcinoma of the parathyroid glands.

Although primary hyperparathyroidism initially exists as a disease entity without complication, it has

Persistent hypercalcemia remains the only readily available, accurate laboratory determination in the diagnosis of primary hyperparathyroidism . . .

been diagnosed because of its complications. Among the recognized complications in the order of frequency are calcification in the urinary tract, decalcification of bones, mental symptoms, peptic ulceration of duodenum or stomach and pancreatitis. The use of routine, laboratory screening of asymptomatic patients has made it possible to detect primary hyperparathyroidism before the complications set in. The incidence of primary hyperparathyroidism appears to be "epidemic" in prevalence. This contribution records the experience in primary hyperparathyroidism at the Washington Hospital Center.

Materials And Methods

Primary hyperparathyroidism was documented in 33 patients at the Washington Hospital Center between March 1969 and March 1973. The following clinical data were evaluated: age, sex, race, presenting symptoms, physical examination, associated conditions, operative findings, pathologi-

cal findings and postoperative course. The following laboratory data were evaluated: serum calcium and phosphorus, uric acid, alkaline phosphatase, electrolytes, hemoglobin, hematocrit, thyroid function studies; urinary calcium, phosphorus, creatinine, and spot urinary calcium. The two highest and two lowest values of the preoperative and postoperative serum calcium and phosphorus were selected in each patient for evaluating the extreme values.

In the Washington Hospital Center clinical laboratory, the serum calcium is determined by the autoanalyzer using the technique described by Kessler and Wolfman (N.V. 9.4-10.6 mg%).^{1,7} For the phosphorus determination a modification of the technique described by Fiske and Subbarow was utilized (N.V. 3-4.5 mg%).^{1,1} The same techniques are used for urinary determination of calcium and phosphorus (N.V. calcium = 100-300 mg/24 hrs; phosphorus = 600-1100 mg/24 hrs). Spot urinary determinations of calcium and creatinine were done and were plotted against a simultaneously determined serum calcium on a graph that relates values of calcium in glomerular filtrate with serum calcium values.^{2,0} This graph helps separate patients with hyperparathyroidism and patients who are euparathyroid or hypoparathyroid. Tubular reabsorption of phosphorus

PRIMARY HYPERPARATHYROIDISM

MISPIRETA, DOROMAL AND DIAZ

was calculated on the basis of 24 hour collection of urine and mid collection specimen of serum phosphorus and creatinine.

The radiologic evidence of bone resorption, urinary tract calcifications, metastatic calcifications and localization of adenomas by cervical esophagogram or arteriogram were reviewed.

The pathological examination of the specimen consisted of measuring the size and weight and specific pathologic diagnosis.

The location of the tumor, number of glands visualized and biopsied during the operative procedure were reviewed. All postoperative complications were recorded.

Results

The increased incidence of primary hyperparathyroidism at the Washington Hospital Center during the recent years probably represents a better understanding and awareness of the disease. (Table 1) There were seven cases of primary hyperparathyroidism from 1959 to 1969. However from

1969 to 1973, 33 cases were documented to have the disease. As in most series, primary hyperparathyroidism was seen more in female patients (57.5%) than in male patients (42.42%). (Table 2)

Sixteen patients (48.48%) had arterial hypertension. Eleven of 33 patients (33.33%) had a history of urinary calculus, six of them recurrent urolithiasis. The next most common complaint was cerebral in origin (30.3%); ten had weakness and fatigue, eight had mental confusion, lethargy and hallucinations. Three patients later went into coma. Three patients (9.09%) had history of polydypsia and polyuria. (Table 3) Three had incidental findings of hypercalcemia while being treated for other conditions. Two patients had parathyroid adenomas which were incidental findings at surgery, one during a thyroidectomy and the other during a lymph node biopsy as part of a work up of hemoptysis. However, there were no preoperative serum calcium determinations. These patients were not included in this study.

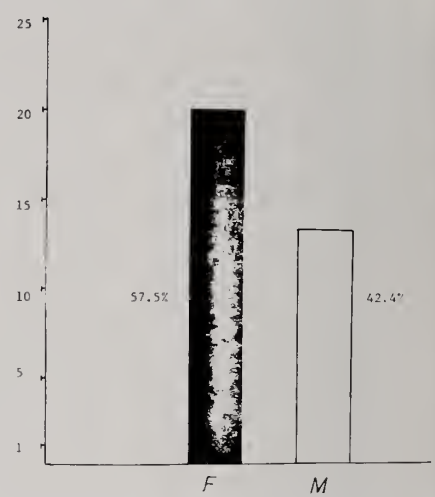


TABLE 2. Sex Distribution Washington Hospital Center 1969-1973

Associated Diseases: Eight patients (24.24%) had peptic ulcer disease, two of whom developed gastrointestinal hemorrhage, one with perforation and one had stomal ulcer following a Billroth II gastrectomy. Nine patients with hyperparathyroidism were investigated for gallbladder disease using oral cholecystography and/or intravenous cholangiography. Six patients (18.1%) had biliary tract disease. Of these, four patients had clinical evidence of gallbladder disease; two patients had acute cholecystitis, one patient had acute suppurative cholangitis and one had chronic cholecystitis and cholelithiasis. Two asymptomatic patients had abnormal gallbladder series. Five patients (15.1%) had thyroid gland abnormalities, one patient with follicular adenocarcinoma, two patients with nontoxic nodular goiter, one patient with follicular adenoma and one patient with colloid cyst. One patient had an adrenal cortical adenoma and another patient had concomitant Addison's disease. Four patients had clinical evidence of arthritis. Two of these were first evident at the time of hospitalization; one was classified as

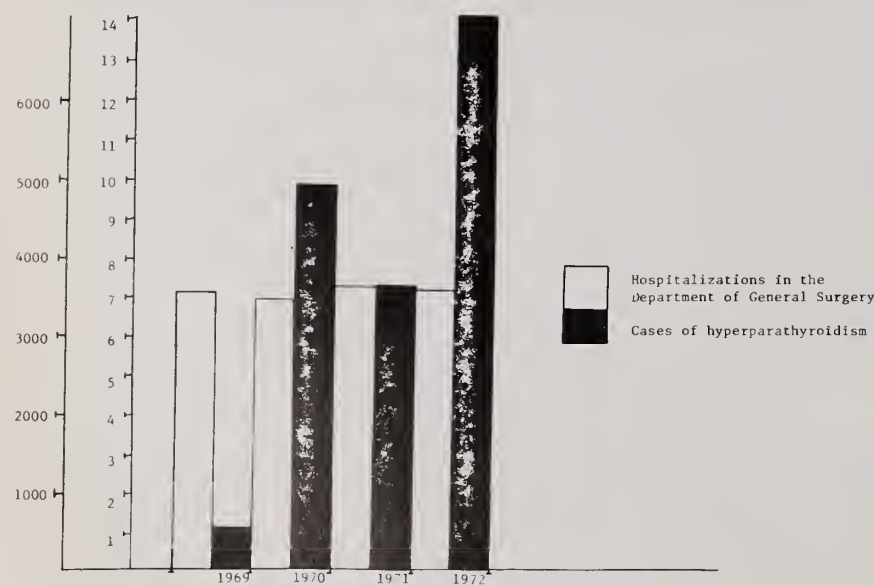


TABLE 1. Annual Incidence of Hyperparathyroidism at the Washington Hospital Center

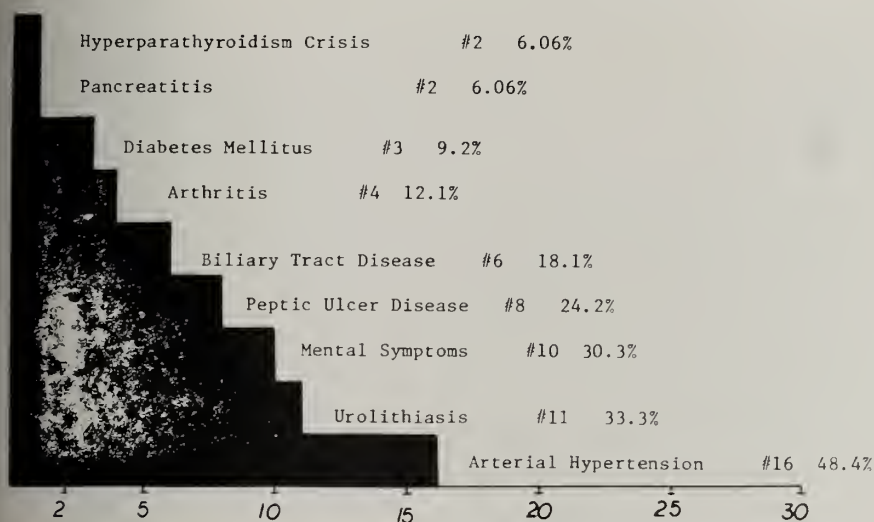


TABLE 3. Clinical Picture Washington Hospital Center 1969-1973

pseudogout and the second was the chief complaint on a patient with hyperparathyroid crisis. The two remaining patients had rheumatoid arthritis. Three patients had associated diabetes mellitus and two other patients presented with acute pancreatitis on admission. Eight (24.2%) patients had a palpable mass in the neck. In six patients the mass was the parathyroid adenoma giving an accuracy rate of 75%.

Laboratory Findings: The hemoglobin ranged between 9.9 to 15 mg% with a mean of 12.8 mg%. The hematocrit ranged between 30.0 and 46.1 with a mean of 40.1. Serum sodium fell between 132 and 148 mEq/L (N.V. 135-147 mEq/L) with a mean of 139.4 mEq/L. The serum potassium was between 2.8 and 5.5 mEq/l (N.V. 4-5.6 mEq/L) with a mean of 4.2 mEq/L. The chloride was between 84 to 108 mEq/L (N.V. 95-105 mEq/L) with a mean of 106.5 mEq/l. The alkaline phosphatase ranged from 1.4 to 5.9 B.L. units (N.V. 0.8-2.3 B.L. units) with a mean of 2.9 B.L. units. The uric acid ran from 4.2 to 11.1 (N.V. 3-7.5 mg%) with a mean of 6.5 mg%. Thyroid function was evaluated

in 19 patients and all were within normal limits. The preoperative serum calcium had a mean of 12.02 mg% (N.V. 9.4-10.6 mg%) with a mean of high serum calcium concentration (two highest for each patient) of 12.9 mg% and a mean serum low calcium concentration of 11.03 mg%. The values ranged between 8.6 and 25 mg%. The mean value of serum phosphorus was 2.8 mg% (N.V. 3-4.5 mg%) with a mean high (two highest values for each patient) of 3.2 mg%, and a mean low (two lowest values for each patient) of 2.47 mg%. The values ranged between 1.5-5.0 mg%. Twenty-seven patients had 24 hour urinary calcium determinations with a mean of 338.4 mg/24 hrs. (N.V. 100-300 mg/24 hrs). Values ranged from 90-840 mg/24 hrs. Nineteen patients had 24 hour collections of urine for phosphorus determinations with a mean of 724.4 mg/24 hrs. (N.V. 600-1100 mg/24 hrs). Values ranged between 100 to 1848 mg/24 hrs. Eighteen patients had tubular reabsorption of phosphorus determination, four patients had values lower than 70%. Five values were between 70-80% and the remainder were above 80%. In

eleven patients, excretion of calcium in the glomerular filtrate was calculated on the basis of spot calcium and creatinine urinary determination. This value was plotted against a simultaneously determined serum calcium. All eleven cases fell in the hyperparathyroid group. (Table 4) Ten patients (30.3%) showed evidence of demineralization of the bone on X-ray. (Figure 1) Eight cases (24.2%) had radiological evidence of urolithiasis, two (6%) had calcification of the choroid plexus. Cervical esophagograms were performed in thirteen patients. The adenoma was localized in only one patient. (Figure 2) Arteriograms of the inferior thyroid arteries were done in two instances. A mass was found in both patients. One had an adenoma and the other had hyperplasia. Both patients developed sensory deficits of the upper extremity secondary to brachial plexus injury during transaxillary arteriogram. Included in the preoperative work up of these patients was a careful search for other cause of hypercalcemia such as neoplastic disease, vitamin D intoxication, sarcoidosis, multiple myeloma, hyperthyroidism, milk-alkali syndrome and prolonged immobilization.

Pathology: Chief cell adenoma was found in 28 patients (84.8%). The weight ranged from 0.210 gm. to 16.5 gm. with a mean of 2.7 gm. The size varied from one cm. in diameter to 4.5 cm. Five cases of hyperplasia (15.1%) were encountered. They were classified according to the scheme suggested by Black.² Three patients had the classical chief cell hyperplasia with all the glands enlarged, one of these patients, originally diagnosed as an adenoma, turned out to have nodular hyperplasia. One case of pseudo-adenomatous chief cell hyperplasia was found and one case of the occult group was encountered. At surgery 20 cases of the 33 had all four glands visualized and six of these had a tissue diagnosis in all four glands. Most of

PRIMARY HYPERPARATHYROIDISM

MISPIRETA, DOROMAL AND DIAZ

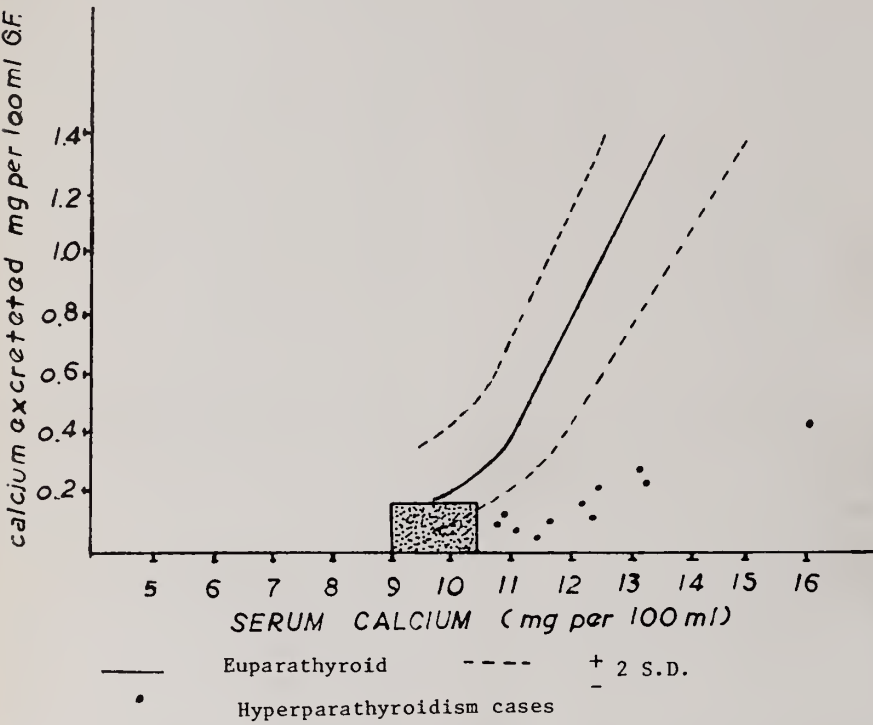


TABLE 4.



FIG. 1. Note the absence of lamina dura and the demineralization of the mandible.

the remaining patients had at least three glands visualized. Of the 28 adenomas, we were able to determine the location in 26. No multiple adenomas were found. Eight had an adenoma of the right inferior parathyroid gland, eight had adenoma of the left inferior parathyroid gland, five in the left superior, three in the right superior and three in the superior mediastinum. (Figure 3)

Postoperative Course: The postoperative serum calcium determinations had a mean value of 8.8 mg%. Values ranged between 6.4 to 11.9 mg%. The postoperative phosphorus determinations had a mean of 3.43 mg% with values ranging between 1.1 to 5.7 mg%. One patient developed hypocalcemia following removal of a parathyroid adenoma and total thyroidectomy for follicular adenocarcinoma. Persistent postoperative hypercalcemia was found in two patients. One patient was re-explored after a negative operation. Selective catheterization of the cervical and mediastinal veins and blood sampling for parathormone was done. An adenoma was found in the left anterior mediastinum. The other patient was first diagnosed as having two chief cell adenomas. Re-exploration of the neck because of persistent hypercalcemia revealed nodular hyperplasia of the remaining glands. The diagnosis of the two first "adenomas" was changed after the slides were reviewed. The postoperative hospitalization period ranged from 3 to 39 days. One patient developed a wound infection due to staphylococcus aureus; another developed a seroma of the incision and one patient died from a perforated peptic ulcer on the twenty-ninth postoperative day.

Discussion

The incidence of parathyroid adenoma and parathyroid hyperplasia in this series parallels the national experi-



FIG. 2. Note extrinsic pressure in the cervical esophagogram (arrow). This corresponded to a 2.5 x 1 cm adenoma (0.8 gm) of the right lower gland.

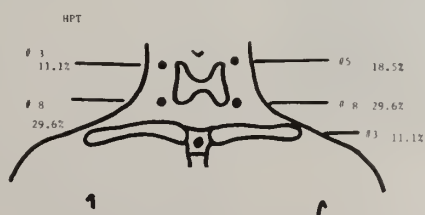


FIG. 3. Localization of Adenomas, WHC 1969-1973.

ence. (Table 5) Carcinoma of the parathyroid gland is reported in most series to be less than one per cent.¹⁵

Parathyroid adenoma is the most common cause of primary hyperparathyroidism. (Figure 4) However, hyperplasia of the parathyroid glands is being recognized more since Cope's description, in 1958, of chief cell hyperplasia.

On the basis of the gross and microscopic morphology, Black² classified thirty-nine cases of primary parathyroid chief cell hyperplasia into three categories. The "classic" group included patients with obvious diffuse enlargement of all parathyroid glands and corresponding microscopic hyperplasia. In the "pseudoadenomatous" group large nodular parathyroids were accompanied by other small glands. The latter, however, were hyperplastic microscopically indicating diffuse abnormality. The third "occult" group was composed of patients whose parathyroid glands were no more than minimally enlarged yet showed microscopic evidence of hyperplasia. (Figures 5,6,7,8)

The detection of asymptomatic primary hyperparathyroidism has been improved by the routine use of laboratory screening by most centers. Almost one half of the cases seen in the University of California Medical Center in the recent years were so diagnosed.¹² The majority of these "asymptomatic" patients on closer scrutiny do have mild complaints.

The most frequent presenting manifestation of primary hyperparathyroidism is urolithiasis. The next most common clinical manifestation is the syndrome made up of hypercalcemia. There is interference with smooth muscle contractility and renal concentrating ability. Higher levels can inhibit neuromuscular irritability and alter cardiac conduction. In early stages, patients have a combination of constipation, anorexia, nocturia, poly-

PRIMARY HYPERPARATHYROIDISM

MISPIRETA, DOROMAL AND DIAZ

TABLE 5. Frequency of Entities Producing Hyperparathyroidism

Author & Date	Institution	Adenomas		Hyperplasia			Unknown	Total
		One Adenoma	Two or More	Chief Cell	Water Clear	Carcinoma		
Cope et al (1958)	Mass. Gen. Hosp.	158(76%)	10(5%)	8(4%)	14(7%)	8(4%)	8(4%)	206
Black, B. M. (1961)	Mayo Clinic	353(92%)	11(25%)	—	19(5%)	2(0.5%)	—	385
Pyrah, et al (1965)	Leeds (England)	60(88%)	4(6%)	2(3%)	3(30%)	—	—	68
Hume (1968)	Med. Coll. of Va.	34(65.38%)	3(5.7%)	10(19.23%)	—	1(1.92%)	4(7.69%)	52
Black, W. C. (1968)	Wash. Univ., St. Louis	21(53.84%)	1(2.56%)	7(17.94%)	—	—	10(25.6%)	39
Cope (1966)	Mass. Gen. Hosp.	263(76.67%)	13(3.79%)	37(10.78%)	15(4.37%)	15(4.37%)	—	343
Mispireta, Doromal & Diaz (1973)	Wash. Hosp. Center	28(84.85%)	—	5(15.1%)	—	—	—	33

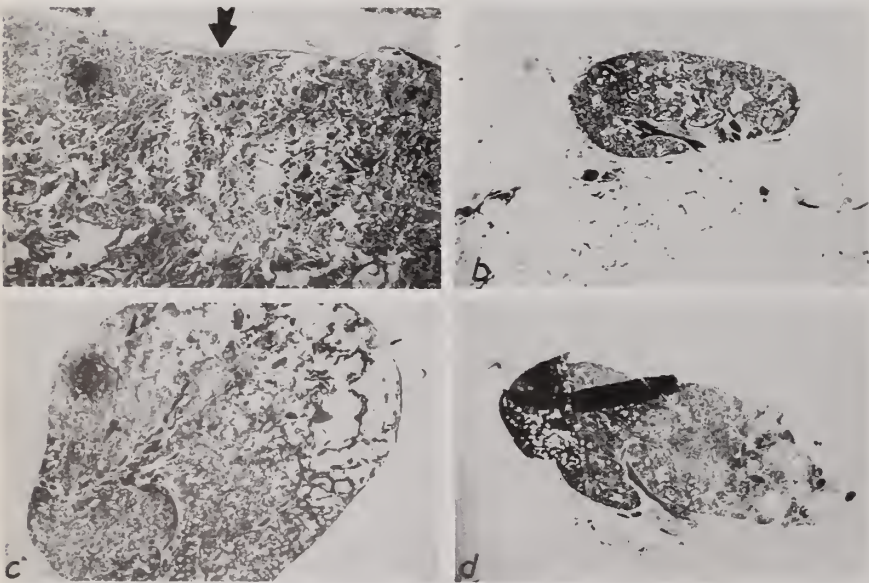


FIG. 4. Adenoma—Note in Figure (a) the presence of a capsule (arrow). Figures (b,c,d) show the other 3 normal glands.

dypsia and polyuria. In later stages, patients develop adynamic ileus, obstipation, nausea, vomiting and abdominal pain. Occasionally psychosis or death can occur.

In about 10% of the patients with primary hyperparathyroidism, peptic ulcer disease develops. This has been attributed to increased secretion of gastrin in hypercalcemia.⁸ In our series 24.4% of our patients had peptic ulcer disease.

Cope and co-workers⁶ first described the relationship between primary hyperparathyroidism and pancreatitis. Several theories have been suggested: 1) precipitation of calcium salts in the pancreatic duct system¹⁹; 2) activation of trypsinogen to trypsin by increased calcium concentration¹⁴; 3) necrosis of pancreatic tissue by the parathyroid hormone⁹; 4) hyperparathyroidism is secondary to the hypocalcemia caused by the release of glucagon from the affected pancreas.¹⁵ Pancreatitis subsided in the two patients in this series after parathyroidectomy.

Hypertension was noted by Hellstrom and Ivemark in 67%¹⁵ and Pyrah²² and associates in 28%. In our series 48.4% have hypertension. Hypertension can be secondary to renal

disease found in some patients. Madhaven and his co-workers¹⁸ attributed hypertension to hypercalcemia.

In rare cases primary hyperparathyroidism may be complicated by crisis characterized by fulminant symptoms of hypercalcemia.³ Abdominal and central nervous system symptoms are most prominent. If untreated the condition progresses to hyperpyrexia and peripheral circulatory collapse and death. In this series two patients with primary hyperparathyroidism died before surgical intervention.

The only accurate way of localizing the adenoma preoperatively is by selective catheterization of the cervical and mediastinal veins and sampling the blood for parathormone. This procedure, however, is not available in most community hospitals so the operating surgeon must be thoroughly familiar with the disease to cope with the problem.

Definitive treatment consists of a thorough surgical exploration of the neck, tracheo-esophageal and retro-esophageal area, and mediastinum. Medical treatment has been tried but is not curative and not capable of reducing a high serum calcium in hypercalcemic crisis.

Calcitonin, a hormone liberated by the C-cells of thyroid glands in response to hypercalcemia, has been used in the treatment of chronic and acute hyperparathyroidism. Calcitonin acts by inhibiting bone absorption and by increasing phosphate excretion in the urine. In adults, administration of calcitonin has a hypocalcemic effect in the presence of active osteolytic bone disease.⁴ Copp reported the diuretic actions of calcitonin.⁷ He has also shown in clinical experiments that calcitonin may be used in the treatment of osteolytic bone diseases and in the treatment of hypercalcemia due to osteolytic bone metastasis. Sorensen and Hindberg found that prolonged calcitonin administration pro-

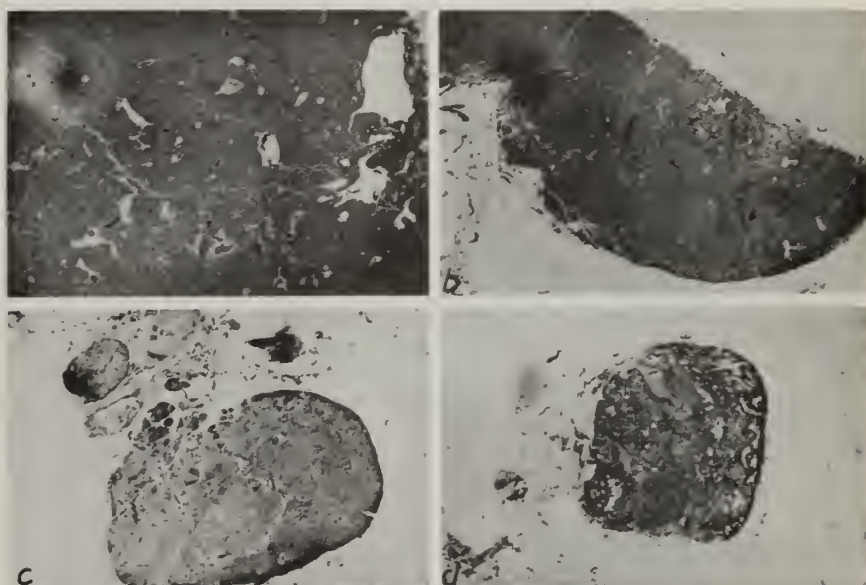


FIG. 5. Chief cell hyperplasia (classical group) Note marked enlargement of two glands (a,b) and moderate enlargement of the remaining two (c,d) All four glands show microscopic evidence of hyperplasia, great cellular density, decreased fat content.

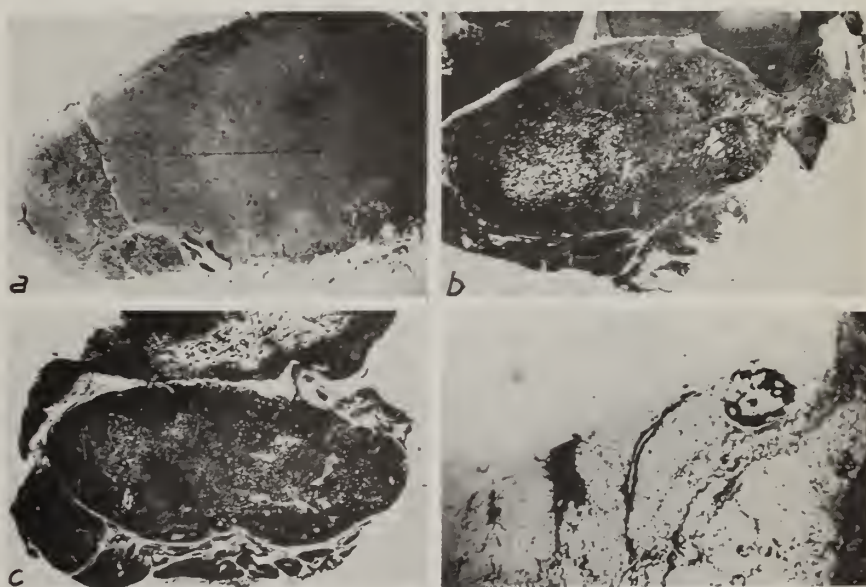


FIG. 6. Chief cell hyperplasia. Classical group, nodular variety. Note enlargement of the glands (a,b,c). All glands, including the biopsy of the fourth gland (d) show evidence of hyperplasia. Note the formation of nodules in 3 of the glands and the formation of rims of parathyroid tissue around them, these rims are of hyperplastic parathyroid tissue which helps to differentiate from adenomas.

PRIMARY HYPERPARATHYROIDISM

MISPIRETA, DOROMAL AND DIAZ

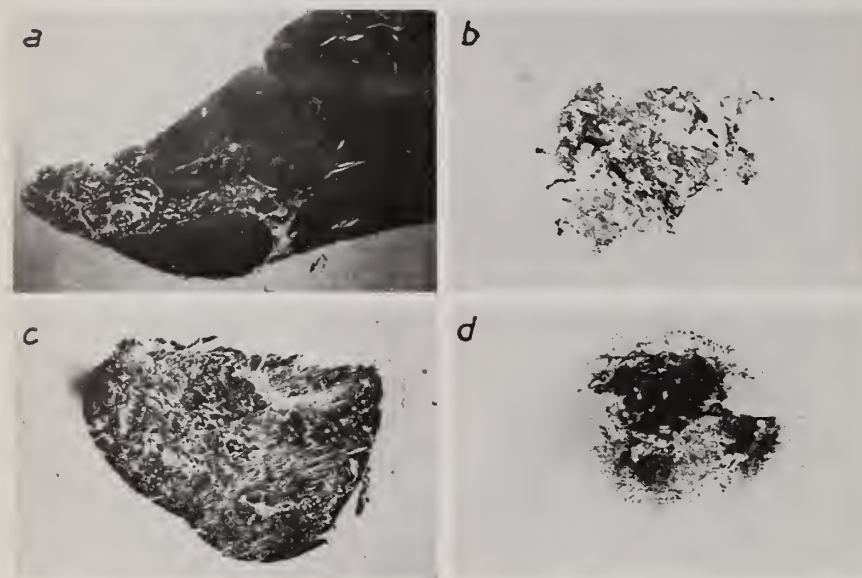


FIG. 7. Chief cell hyperplasia, pseudo adenomatous group—enlargement of one gland (a) with remaining glands of normal size was present at the time of surgery. Two glands were removed completely (a,c) and two partially (b,d). Note microscopic evidence of hyperplasia in all four.

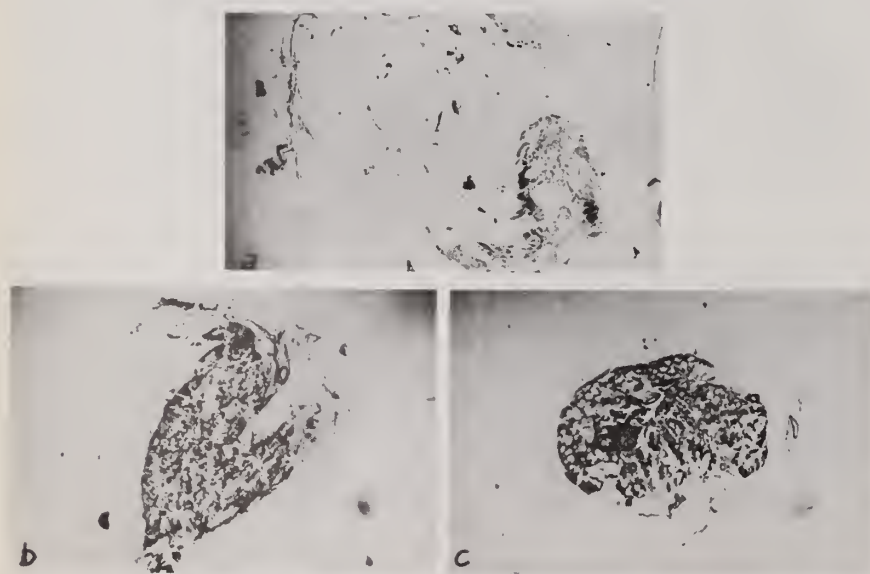


FIG. 8. Chief cell hyperplasia occult group. All glands were found to be of normal size at the time of surgery. Three glands were removed. Note subtle microscopic changes of hyperplasia. Hypercalcemia corrected after surgery.

duced a secondary hyperparathyroidism.^{2,3} The real value of calcitonin in primary hyperparathyroidism is still under investigation.

The surgical removal of the abnormally functioning parathyroid gland remains the only treatment of primary hyperparathyroidism. This treatment must be instituted as soon as the diagnosis is made especially in hypercalcemic crisis.

The practice at the Washington Hospital Center is to thoroughly explore the neck and positively identify all four glands. If an enlarged gland is visualized, this is removed and a biopsy is taken from each normal appearing gland. If an adenoma is found and the biopsies prove to be normal glands, the operation is terminated. If the gland and the biopsy show hyperplastic changes then a near total parathyroidectomy is performed.

If no adenoma is found in the usual places, the retrotracheal and esophageal areas are explored. Following this the superior mediastinal area is explored through the same incision. Goldman *et al*¹² were able to remove 98% of the adenomas through the cervical incision. A subtotal thyroidectomy is performed if all efforts are fruitless.

Paloyan²¹ advises a near total parathyroidectomy leaving only 50-60 mg. of well-vascularized tissue because of an unacceptable number of recurrent hypercalcemia. However, Egdahl¹⁰ recommends that no more than 30 mg. of tissue be left. Ballanger reported in his series of 74 patients, a 13% incidence of recurrent hypercalcemia.¹³ He attributes this high incidence rate to difficulty in differentiating between adenoma and hyperplasia. Supporting this, Saul Kay¹⁶ states "In the absence of the capsule, the adenoma and hyperplastic gland can be histologically identical, and we

would defy anyone to separate them when received as unknown specimens." Later in the same paper it is stated "since most of our surgeons attempt to view and perform biopsies on all four glands, we are presented with the most reliable feature of separating the adenoma from hyperplasia."

References.

1. BEAHR, O. H., ANGELOS, S. P., WOOLNER, L. B.: Carcinoma of parathyroid gland. Report of a Case. *Surg. Clinic of N. America*, 1963, 43: 1123.
2. BLACK, W. A., HAFF, R. C.: The surgical pathology of parathyroid chief cell hyperplasia. *Am. J. Clin. Path.*, 1970, 53: 565.
3. BOQUIST, L., BERGDAHL, L., ANDERSSON, A.: Parathyroid adenoma complicated by acute hyperparathyroidism. *Ann. Surg.*, 1971, 173: 593.
4. BURCHARTH, F., CASTBERG, T., VIBE-HANSEN, H.: Problems in primary hyperparathyroidism. *Surg. Gynec. & Obstet.*, 1972, 135: 397.
5. COPE, O., NARDI, G. L., CASTLEMAN, B.: Carcinoma of the parathyroid gland. Four cases among 143 patients with hyperparathyroidism. *Arch. Surg.*, 1953, 138: 661.
6. COPE, O., CULVER, P. J., MIXTER, G. G. Jr., NARDI, G. L.: Pancreatitis, a diagnostic clue to hyperparathyroidism. *Ann. Surg.*, 1957, 145: 857.
7. COPP, D. H.: Calcitonin and calcium metabolism. *Canad. Med. Assoc. J.*, 1970, 103: 821.
8. DENT, R. I. *et al*: Hyperparathyroidism: Gastric acid secretion and gastrin. *Ann. Surg.*, 1972, 176: 360.
9. DREILING, D. A.: The pathological physiology of pancreatic inflammation. *J.A.M.A.*, 1961, 175: 105.
10. EGDAHL, R. H.: Personal communication.
11. FISKE, SUBBAROW. J. *Biol. Chem.*, 1925, 66: 375.
12. GOLDMAN, L., GORDAN, G. S., ROOF, B. S.: The parathyroids: Progress, Problems and Practice. *Current Problems in Surgery*, Aug. 1971.
13. HAFF, R. C., BALLANGER, W. F.: Causes of recurrent hypercalcemia after parathyroidectomy for primary hyperparathyroidism. *Ann. Surg.*, 1971, 173: 884.
14. HAVERBACK, B. J., DYCE, B., BUNDY, H., EDMONDSON, H. A.: Trypsin, trypsinogen and trypsin inhibitor in human pancreatic juice. *Am. J. Med.*, 1960, 29: 424.
15. HELLSTROM, J., IVEMARK, B. I.: Primary hyperparathyroidism. *Acta Chir. Scandinav.*, 1962, Suppl. 294: 1.
16. KAY, S.: Primary hyperparathyroidism as observed over a 22 year period. *Arch. Pathol.*, 1973, 95: 256.
17. KESSLER, WOLFMAN: *Clin. Chem.*, 1964, 10: 686.
18. MADHAVEN, T., FRAME, B., BLACK, W. A.: Influence of surgical correction of primary hyperparathyroidism on associated hypertension. *Arch. Surg.*, 1970, 100: 212.
19. MIXTER, C. G. Jr., KEYNES, W. M., COPE, O.: Further experience with pancreatitis as a diagnostic clue to hyperparathyroidism. *New Engl. J. Med.*, 1962, 266: 265.
20. NORDIN, B. E., BULUSU, L.: A modified index of phosphate excretion. *Postgrad. Med. J.*, 1968, 44: 93.
21. PALOYAN, E., PALOYAN, D., PICKLEMAN, J. R.: Hyperthyroidism today. *Surg. Clinic of N. America*, 1973, 53: 211.
22. PYRAH, L. N., HODGKINSON, A., ANDERSON, C. K.: Primary HPT. *Brit. J. Surg.*, 1966, 53: 245.
23. SORENSEN, O. H., HINDBERG, T.: Calcitonin and bone. *Lancet*, 1970, 1: 1061.

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THE VIEW BOX

Prepared by
The Department of Radiology
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A young lady had a chest radiograph as part of a college entrance examination. This showed an "abnormality." She was asymptomatic and the clinical examination revealed no significant findings. (for diagnosis see page 333)



Mesenteric Vascular Disease: Clinical Features and Review of the Literature

ALBERTO J. MUNIAGURRIA, M.D. AND ALLENDER SYBERT, M.D.

Mesenteric vascular disease should be included in the differential diagnosis of all cases of abdominal pain of obscure etiology, especially in the setting of diffuse arteriosclerosis, myocardial infarction or hypoperfusion states.

Abstract

The clinical, laboratory and pathologic features of 13 cases of mesenteric vascular disease are reviewed, and four illustrative cases are reported. The characteristics of chronic intestinal ischemia and the various types of acute intestinal infarction, as described in the literature, are reviewed. The importance of early diagnosis and prompt therapeutic intervention is emphasized.

Introduction

Mesenteric vascular disease includes chronic intestinal ischemia and acute intestinal infarction. The latter may be caused by mesenteric arterial or venous thrombosis, or by arterial embolism, or may occur without demonstrable vascular occlusion¹.

These serious conditions are often unrecognized on medical wards, and, when not recognized and treated early enough, often result in death due to intestinal infarction. Consequently, a high index of suspicion is necessary. These conditions should be included in the differential diagnosis of abdominal pain without clear origin.

Difficulties in recognizing these not uncommon diseases prompted a review of the clinical manifestations and methods employed in the diagnosis of mesenteric vascular disease.

Methods

The records of patients suspected of having mesenteric vascular disease who were seen between 1966 and 1973 at Georgetown University Hospital were reviewed. In thirteen cases the diagnosis was confirmed by x-ray, surgery or autopsy examination. Patients suspected of having mesenteric vascular disease without confirmation by one of the above methods were excluded.

Results

The clinical, laboratory, roentgenographic and pathologic findings in 13 patients with mesenteric vascular disease are summarized in Table 1.

Characteristics of Patients. One patient was 30 years of age, the others ranged in age from 52 to 87 years.

There were six men and seven women. Twelve were white, one black.

A diagnosis of coronary or peripheral arteriosclerosis had been made in 11 of the 13 patients. Four had a history of carcinoma, three were in shock due to hemorrhage or sepsis, three had had a recent or remote myocardial infarction, three were in atrial fibrillation, and two in heart failure.

Symptoms and Signs. One patient (K.P.) presented with typical features of chronic intestinal ischemia and underwent elective surgery with a successful result. The remaining 12 patients had acute intestinal infarction. Of the 12, 10 presented with abdominal pain, six had nausea and/or vomiting, and three complained of diarrhea.

The most common physical findings in the patients with acute intestinal infarction were abdominal tenderness and hypoactive bowel sounds. Abdominal distension and rebound tenderness were also commonly present.

Laboratory Findings. The white blood cell count was below 12,000 per mm³ in 2 of the 12 patients with intestinal infarction, 12,000 to 20,000 in three patients, and ranged from 24,300 to 43,000 in the other seven patients. The serum amylase was normal in four of the 10 patients in whom it was tested, and was elevated in six patients, ranging from 157 to 450

TABLE 1. Summary of findings in 13

Patient	Age & Sex	Race	Underlying Disease	Symptoms	Physical Signs	WBC per mm ³
K.P.	60, F	W	Arteriosclerosis	Abdominal pain, weight loss	Systolic murmur, epigastric bruit, diminished pulses	10,400
J.H.	68, M	B	Arteriosclerosis	Abd. pain, nausea, vomiting	Hypertension, abd. tender- ness, femoral bruits, systolic murmur	24,300
H.P.	70, M	W	Carcinoma of the tongue	Abd. pain, nausea	Abd. distension, diffuse ten- derness, hypoactive bowel sounds	7,700
M.M.	75, F	W	Arteriosclerosis, carcinoma of the colon, hemorrhagic shock	Confusion, dis- orientation	Abd. distension, tenderness	12,000
M.W.M.	30, M	W	Gastric ulcer with hemorrhage and shock	Abd. pain, nausea, diarrhea, hema- temesis	Cyanosis, coma, abd. disten- sion, absence of bowel sounds	43,000
M.S.	73, F	W	Arteriosclerosis	Abd. pain, weight loss, diarrhea	Systolic murmur, diminished pulses	25,200
C.P.	58, M	W	Arteriosclerosis, myocardial infarction, bronchogenic carcinoma, hypotension	Weakness, dyspnea	Abd. tenderness, direct & re- bound, hypoactive bowel sounds	37,600
H.W.	67, F	W	Arteriosclerosis, heart failure, atrial fibrillation	Crampy abd. pain, diarrhea, vomiting	Abd. distension, direct & re- bound tenderness, hypoactive bowel sounds	29,400
G.I.	87, F	W	Arteriosclerosis, aortic stenosis	Abdominal pain	Tachycardia, systolic & diastolic murmurs, diminished pulses, hypoactive bowel sounds	10,900
E.C.	63, F	W	Arteriosclerosis, atrial fibrillation, shock	Diffuse abd. pain	Tachycardia, hypotension, cyanosis, abd. tenderness, hypoactive bowel sounds	28,000
J.M.H.	59, M	W	Arteriosclerosis, myocardial infarction, heart failure	Abd. pain, diaphoresis	Generalized abd. tenderness, absence of bowel sounds	25,000
P.P.	52, M	W	Arteriosclerosis, myocardial infarction, atrial fibrillation	Abd. pain, nausea, vomiting	Tachycardia, cyanosis, dimin- ished pulses, abd. tenderness, hypoactive bowel sounds	18,000
L.P.	73, F	W	Arteriosclerosis, carcinoma of the pancreas	Epigastric pain, nausea, vomiting	Abd. distension, direct & rebound tenderness, hypo- active bowel sounds	18,300

W = white

B = black

WBC = white blood cell count

N.R. = not recorded

+ = positive for blood

- = negative for blood

SMA = superior mesenteric artery

units per 100 cc. In six of the 12 patients with infarction, the hematocrit rose during the course of the disease.

Gastric contents were positive for blood in all seven of the patients tested by guaiac, and rectal contents were positive in seven of the eight patients tested. Abdominal paracentesis yielded bloody fluid in four of the five cases in which it was performed.

Abdominal roentgenograms showed a non-specific intestinal gas pattern consistent with paralytic ileus in 10 of the 11 cases of intestinal infarction in which films were obtained. In only one case (G.I.) did the films show gas within the intestinal wall and in the portal venous system (Figures 1 to 3).

Pathologic Findings. Of the 12 patients with acute intestinal infarction only one survived. In that case the presence or absence of vascular occlu-

sion could not be determined from the surgical specimen. Of the 11 patients who died, four had superior mesenteric artery thrombosis and three had mesenteric venous thrombosis. In three patients no vascular occlusion was found. In one case postmortem examination was not performed, and the etiology of the intestinal infarction could not be determined. There were no cases of mesenteric embolism, and no cases of inferior mesenteric artery

patients with mesenteric vascular disease

Serum Amylase (U./100 cc)	Rise in Hematocrit	Gastric Guaiac	Rectal Guaiac	Abdom. Tap	Roentgen Findings	Survival	Pathologic Findings
N.R.	no	N.R.	N.R.	N.R.	Arteriography: partial occlusion of SMA	yes	SMA obstruction without intestinal infarction
235	no	N.R.	N.R.	N.R.	Gas in small bowel	no	SMA thrombosis with infarction
56	no	N.R.	N.R.	N.R.	Gas in small bowel	yes	Infarction of ileum
69	no	+	+	N.R.	Gas in small bowel	no	Infarction of ileum without vascular occlusion
298	no	+	+	Bloody	Gas in small bowel	no	Mesenteric & portal venous thrombosis with infarction of small intestine
310	yes	+	+	Bloody	N.R.	no	SMA thrombosis with infarction of the small intestine
450	yes	N.R.	—	Bloody	Gas in small bowel	no	SMA thrombosis with infarction of small & large bowel
N.R.	yes	+	+	N.R.	Gas in small bowel	no	Infarction of ileum & jejunum without vascular occlusion
N.R.	yes	+	+	N.R.	Gas in small bowel lumen & wall & in-portal veins	no	N.R.
250	no	+	+	Not bloody	Dilated stomach	no	Infarction of small and large bowel without vascular occlusion
129	yes	N.R.	N.R.	Bloody	Gas in small bowel	no	Mesenteric venous thrombosis with infarction of jejunum, ileum & ascending colon
157	yes	N.R.	N.R.	N.R.	Gas in small bowel	no	Mesenteric venous thrombosis with infarction of small bowel
75	no	+	+	N.R.	Gas in small bowel with air-fluid levels	no	SMA thrombosis with small bowel infarction

thrombosis. Pathologic specimens from a case of mesenteric venous thrombosis are pictured in Figures 4 and 5.

Case Reports

Case 1 (GUH #253522). This sixty year old white woman (K.P.) entered Georgetown University Hospital because of a history of 18 months of mid-epigastric pain, which began

shortly after eating. During that time she lost 27 pounds. She denied nausea, vomiting or diarrhea. She had intermittent claudication in both legs after walking a few blocks. A selective mesenteric arteriogram was performed at another hospital. It showed partial obstruction of the superior mesenteric artery. She was referred to Georgetown for corrective surgery.

On physical examination her blood pressure was 145/95 mm Hg., her

pulse 94 beats per minute and regular, and her weight 81 pounds. A grade III/VI systolic murmur at the left sternal border radiated to the apex. The abdomen was soft, with no tenderness but with generalized discomfort on palpation. There was a bruit in the epigastrium, radiating toward the right lower quadrant. The popliteal and posterior tibial pulses were diminished.

The hematocrit was 34.5%, the

MESENTERIC VASCULAR DISEASE

MUNIAGURRIA AND SYBERT



FIG. 1. Supine abdominal film in a case of acute intestinal infarction demonstrates dilated, gas-filled loops of small and large bowel. In addition, gas can be seen within the portal venous system (upper arrows), and a cleft-like distribution of gas is present in the wall of the bowel (lower arrows). The latter features are virtually diagnostic of intestinal infarction.

white blood cell count 10,400 per mm^3 with 49% segmented forms, 6% bands and 36% lymphocytes. The blood urea nitrogen was 10 mg. per 100 cc., and the serum creatinine 0.4 mg. per 100 cc. The urinalysis was within normal limits. Serum cholesterol and triglyceride levels were normal. Chest roentgenograms showed no evidence of active pulmonary disease.

At operation the superior mesenteric artery was found to be obstructed at a point one and one half centimeters distal to its origin from the aorta. The obstruction was bypassed with a segment of the superficial saphenous vein from the left thigh. The postoperative course was uneventful and the patient was discharged 15 days after admission.

Comment: This is a typical case of chronic intestinal ischemia, and illustrates the features of recurrent postprandial pain and weight loss in a patient with evidence of generalized atherosclerosis. The proximal location of the obstructing plaque makes it suitable for surgical correction.

Case 2 (GUH #195519). This 68 year old black man (J.H.) entered Georgetown University Hospital with severe epigastric pain of six hours duration. Six weeks prior to his admission he had been admitted to another hospital with the complaint of severe abdominal pain of sudden onset. He was diagnosed and treated as a myocardial infarction, though there were no changes in the electrocardiogram. He was found to have a microcytic hypochromic anemia. He was discharged on iron therapy. The patient had been at home for one week, doing well, until the morning of his admission to Georgetown, when, after a meal, he developed severe incapacitating abdominal pain radiating to the left leg. The pain was accompanied by nausea and vomiting. He had had a normal bowel movement on the morning of admission.

Physical examination on admission showed a blood pressure of 200/110 mm Hg., pulse 60 beats per min. and regular, respirations 25 per minute and labored. There was a grade III/VI systolic murmur at the apex, radiating to the axilla. The lungs were clear. There was marked abdominal tenderness to light palpation, with guarding throughout the abdomen. The bowel sounds were normal. There were bilateral femoral bruits.

The hematocrit was 32.5 per cent and the white blood cell count 24,300 per mm^3 with 81% segmented forms, 11% bands, 7% lymphocytes and 1% monocytes. The urinalysis was within normal limits. The blood urea nitrogen was 16 mg. per 100 cc., serum creatinine 1.9 mg. per 100 cc., serum amylase 235 units per 100 cc.

The electrocardiogram showed right bundle branch block. The chest roentgenogram showed mild cardiomegaly without evidence of active pulmonary disease. Supine and erect films of the abdomen were normal on the day of admission, but on the following day gas was present in the small bowel.

On the second hospital day he developed more intense upper abdominal tenderness with rebound tenderness and hypoactive bowel sounds. An exploratory laparotomy was then performed. Thrombosis of the superior mesenteric artery was found, with intestinal infarction extending from the ligament of Treitz to the descending colon. The infarcted segment of bowel was resected and a duodenosigmoidostomy was performed. The postoperative course was complicated by progressive renal failure. On the eighth postoperative day the patient died.

Comment: The severe abdominal pain, the development of signs of peritonitis, and the non-specific abdominal roentgenographic picture are typical of acute intestinal infarction. The extent of intestinal necrosis in this case corresponds to the area supplied by



FIG. 2. Detail from Figure 1, showing gas distributed within the intrahepatic radicles of the portal venous system (arrows).



FIG. 3. Detail from Figure 1 showing a cleft-like distribution of gas within the intestinal wall (arrows).

MESENTERIC VASCULAR DISEASE

MUNIAGURRIA AND SYBERT



FIG. 4. Postmortem specimen in a case of mesenteric venous thrombosis (P.P.), showing thrombi within the mesenteric veins (arrows).

the superior mesenteric artery. Whether the episode of epigastric pain six weeks earlier and the anemia were manifestations of chronic intestinal ischemia with occult blood loss is open to speculation.

Case 3 (GUH #181133). This 30 year old white man (M.W.M.) was admitted to another hospital with a history of three days of generalized abdominal pain, nausea, and loose watery stools. Physical examination showed a minimally distended but otherwise unremarkable abdomen. The white blood cell count was 15,000 per mm^3 on admission. Roentgenographic studies of the gall bladder and upper gastrointestinal tract were interpreted as normal, and the serum amylase was normal. The diagnosis of gastroenteritis was entertained. He was treated with analgesics for three days with only partial relief of his pain. Because the degree of his subjective discomfort did not appear to correlate with his unremarkable abdominal examination, a psychiatric consultation was obtained. A diagnosis of schizoid affective disorder was made, and the patient was transferred to the psychiatric unit.

On the ninth day after the onset of his symptoms he had seven episodes of hematemesis, and his blood pressure was unobtainable. He was treated with intravenous fluids. The abdominal examination was still unrevealing and roentgenograms of the abdomen were normal. On the following day he was semi-comatose, the blood pressure was 90/60 mm Hg. and the pulse 150 beats per minute. The bowel sounds were absent. He became oliguric and finally anuric. Attempts at improving urine output were unsuccessful and by the end of the second day after the onset of hematemesis he was unresponsive with a blood urea nitrogen of 166 mg. per 100 cc. The hematocrit was 50% and the white blood cell count 30,000 per mm^3 with 77% segmented forms

and 13% bands. The blood urea nitrogen rose to 216 mg. per 100 cc. with the serum creatinine 7 mg. per 100 cc. At that point he was transferred to Georgetown University Hospital for further evaluation and for hemodialysis.

On admission the patient was cyanotic and unresponsive with a blood pressure of 130/80 mm Hg. and a pulse of 180 beats per minute. There was dullness on percussion at the right lung base. A grade II/VI systolic murmur at the left sternal border radiated to the axilla. The abdomen was distended with tympany in the right hypochondrium. No bowel sounds were present.

The hematocrit was 37% and the white blood cell count 43,000 per mm³. Serum electrolytes were normal, blood urea nitrogen was 230 mg. per 100 cc. and arterial blood pH 7.57. Urinalysis showed 1+ albumin and granular casts. Nasogastric suction yielded bloody fluid. Rectal contents were guaiac positive. A chest roentgenogram showed an elevated right hemidiaphragm.

Hemodialysis was performed for two hours. The patient was then taken to the operating room where an exploratory laparotomy revealed an actively bleeding gastric ulcer, which was oversewn. A large segment of the small intestine was noted to be necrotic and was resected. Two hours after termination of surgery the patient died. The autopsy findings included hemoperitoneum with fibrinous peritonitis and thrombosis of the portal, mesenteric, splenic and pancreatic veins.

Comment: The early stage of this patient's illness was characterized by severe abdominal pain without abnormalities on physical examination. He later developed severe shock secondary to a bleeding gastric ulcer. The extensive venous thrombosis was perhaps related to prolonged hypotension.

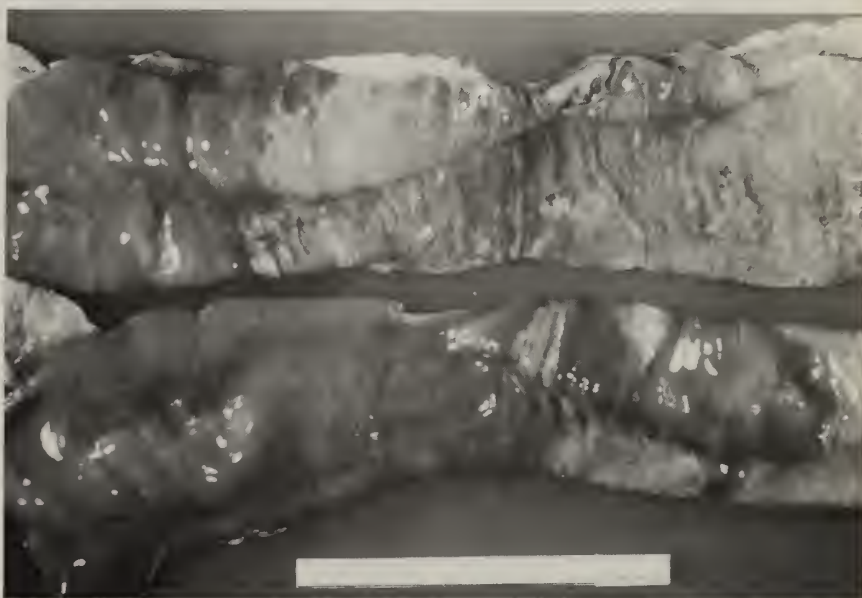


FIG. 5. Postmortem specimen of infarcted small intestine in a case of mesenteric venous thrombosis (P.P.).

Case 4 (GUH #057501). This 63 year old white woman (E.C.) had a history of coronary artery disease and chronic atrial fibrillation, treated with digitalis. Ten days prior to her admission an abdominal hysterectomy for cystic hyperplasia had been performed at another hospital. After surgery she complained of diffuse crampy abdominal pain. There was no nausea, vomiting or diarrhea. A low grade fever rose to 102° F. orally. She soon became hypotensive and oliguric, and was treated with metaraminol and isoproterenol, in addition to penicillin, kanamycin, and corticosteroids. She was transferred to Georgetown University Hospital.

Her past medical history included peptic ulcer disease and hepatosplenomegaly of many years' duration without definite diagnosis.

Physical examination revealed a thin white woman, oriented but with cold clammy skin. She was dyspneic and in respiratory distress. No blood pressure was obtainable, the pulse was not

palpable. Respiratory rate was 36 per minute, rectal temperature was 100° F. The lips were cyanotic, the pupils were dilated but reactive to light. Diffuse expiratory wheezes were heard in both lung fields. The heart rate was 124 beats per minute with an irregularly irregular rhythm. A healing incision extended from the umbilicus to the pubis. The epigastrium was diffusely tender. There was direct and rebound tenderness of both upper abdominal quadrants. There was no distension. Bowel sounds were hypoactive. The stool was guaiac negative. Neurologic examination was normal.

The hematocrit was 46%, the white blood cell count 28,000 per mm³ with 90% segmented forms. The serum sodium was 128 mEq/L., blood urea nitrogen 50 mg. per 100 cc., and serum amylase 250 units per 100 cc. The urinalysis showed a specific gravity of 1.023, 1+ albumin and six red blood cells. Blood cultures were negative. The chest roentgenograms showed no active pulmonary disease.

MESENTERIC VASCULAR DISEASE

MUNIAGURRIA AND SYBERT

An abdominal film showed the stomach to be dilated. The electrocardiogram showed atrial fibrillation.

The patient was treated for shock with intravenous fluids, isoproterenol, corticosteroids and antibiotics. The blood pressure rose to 120/90 mm Hg. She was taken to the operating room the next day.

At surgery the entire small intestine from the ligament of Treitz to the ileocecal valve was dusky in appearance, and there were patchy areas of duskiness in the large bowel. The cecum and a portion of the ascending colon were necrotic and were resected, and a Mikulicz procedure was done. Three days later, with the patient in fairly stable condition, a re-exploration was performed for resection of necrotic bowel. At that time the area of necrosis extended from three inches distal to the ligament of Treitz to the sigmoid colon. Consequently, no further resection was performed, and two days later the patient died.

At autopsy massive hemorrhagic infarction of the ileum, colon and rectum was found. The mesenteric vessels at operation and at autopsy were found to be patent.

Comment: In this case intestinal infarction without mesenteric vascular occlusion occurred following an episode of hypotension.

Review of Literature

Vascular supply to the abdominal viscera is derived from three unpaired branches of the abdominal aorta, the celiac axis and the superior and inferior mesenteric arteries. Anastomotic connections between the celiac axis and the superior mesenteric artery, and between the superior and inferior mesenteric arteries, provide for the establishment of collateral circulation².

Chronic Intestinal Ischemia

Chronic intestinal ischemia, also termed abdominal or intestinal angina, consists of recurrent attacks of temporary intestinal ischemia, separated by periods in which blood flow is adequate. In this condition, blood flow is sufficient to maintain viability of the bowel, but is insufficient to meet the increased demands on the circulation during digestion³. The insufficiency of blood flow during digestion results in temporary ischemia, which is manifested as abdominal pain.

The term intestinal angina, suggested by Mikkelsen⁴, points out the analogy to angina pectoris: both are examples of ischemic pain, resulting from arterial insufficiency and occurring when the organ is functionally stressed.

Intestinal angina usually results from atherosclerotic narrowing of the celiac axis or superior mesenteric artery³. The obstructing plaque is typically located within 1.5 cm. of the origin of the vessel, making it suitable for surgical correction⁵. The inferior mesenteric artery is less often involved⁶. Infrequent causes of obstruction include celiac axis compression by the celiac ganglion or arcuate ligament of the diaphragm^{7,8}, aortic aneurysm, and periarteritis nodosa⁹.

Because of the presence of anastomotic connections between the vessels supplying the abdominal viscera, it has been postulated that in most cases at least two of the three vessels must be involved before symptoms appear^{3,6,10}.

Clinical Features. Intestinal angina occurs primarily in men in the sixth to eighth decade of life. The cardinal feature of the clinical presentation is postprandial abdominal pain. The pain is described as being sharp, crampy or achy³, may be epigastric⁶ or periumbilical³, and may radiate to the

back¹⁰. The pain begins 15 to 60 minutes after the ingestion of food, and persists for several hours⁶. It may be accompanied by abdominal distension, nausea, vomiting, and either diarrhea or constipation¹⁰. Patients voluntarily decrease their food intake to minimize the pain, and the resulting weight loss may be profound².

Physical examination, even during pain, is often unrevealing, except for the evident weight loss and for signs of arteriosclerosis, such as diminished peripheral pulses⁶. Some patients have an abdominal bruit. Examination of the stool may reveal occult blood and an increased fat content, and significant malabsorption may be present². Gastrointestinal x-ray studies are usually normal, though some patients demonstrate a mucosal pattern suggesting malabsorption².

The diagnosis is confirmed by mesenteric arteriography, including films taken in the lateral projection to demonstrate the origins of the mesenteric arteries¹⁰. Identification of the site of obstruction permits definitive surgical therapy, which, because of the usual proximal location of the lesion, often consists of endarterectomy or bypass grafting. It has been pointed out, however, that the demonstration of an obstructing lesion does not guarantee that relief of the obstruction will eliminate the patient's symptoms¹. Nevertheless, in a patient with the appropriate clinical picture, unexplained by other gastrointestinal diseases, and in whom arteriography has demonstrated significant obstruction of two or more of the mesenteric arteries, chronic intestinal ischemia should be suspected, and corrective surgery should be performed².

Early recognition and prompt surgical correction of this disease is important not only to relieve symptoms, but also to interrupt the natural progression of the disease to intestinal infarction, with its dire prognosis⁶.

Acute Intestinal Infarction

Acute intestinal infarction includes the following separate entities: occlusion of the superior or inferior mesenteric artery by thrombosis or embolism, non-occlusive intestinal infarction, and mesenteric venous thrombosis. All share a similar clinical presentation as an acute abdominal catastrophe and share a poor prognosis unless recognized and treated promptly.

The relative frequency of the various types of intestinal infarction depends on the series being reviewed. In a 1963 review of 1500 cases, Jackson¹¹ found that 33% were due to venous occlusion, 12% to non-occlusive infarction, and the remainder to arterial occlusion, evenly divided between thrombosis and embolism. More recently, Britt and Cheek¹² reported a series of 45 cases of mesenteric infarction of whom 33% had arterial thrombosis, 13% arterial embolism, 36% non-occlusive infarction, and 18% venous thrombosis. Ottinger and Austen¹³ reported a series of 136 patients with mesenteric infarction, 16% of whom had arterial thrombosis, 21% arterial embolism, 49% non-occlusive infarction, and 7% venous thrombosis, with a few cases of infarction secondary to dissecting aortic aneurysm and to arteritis. Ottinger and Austen report an overall incidence of mesenteric infarction of 8.8 per 10,000 admissions. Liavag¹⁴ reports an incidence of 1.7 per 1000 surgical admissions.

Arterial thrombosis is invariably superimposed on an atherosclerotic lesion^{2,13}. Patients generally have evidence of diffuse arteriosclerosis (75% in Jackson's series¹¹), and many have a preceding history of myocardial or cerebral infarction¹¹. According to Williams², the majority of patients

suffering a fatal superior mesenteric artery occlusion have had abdominal angina.

Emboli to the superior mesenteric artery account for 5% of all peripheral emboli³, and usually arise from mural thrombi following myocardial infarction or from atrial thrombi in patients with rheumatic heart disease². Rarely, emboli may result from dislodgement of an aortic atheromatous plaque¹¹ or from vegetative endocarditis. Up to 5% of patients with mesenteric embolism have a prior history of peripheral embolization², and in one series¹¹ 80% of patients with mesenteric embolism were in atrial fibrillation.

Superior Mesenteric Artery Occlusion. The clinical features are similar whether the etiology is thrombosis or embolism, though it has been said that patients with embolic occlusion are somewhat younger and have a more sudden and dramatic onset of symptoms¹⁵.

The initial symptom is abdominal pain, which may be gradual or sudden in onset¹⁵, soon becomes severe, and characteristically is unrelieved by the usual doses of narcotics¹¹. The pain may be crampy or steady, is not well localized¹⁶, and may radiate to the back¹¹. Anorexia and nausea are common, and vomiting occurs in 80 to 90% of cases^{11,14}. Either diarrhea or constipation may be present¹¹ and both gastric and rectal contents may contain blood.

At an early stage, the pathologic features include spasm of the intestinal wall and mucosal infarction¹³, but full-thickness infarction of the intestine has not yet occurred, and peritonitis is not present. Consequently, the physical signs at this stage are minimal, consisting of generalized abdominal tenderness and hyperactive bowel sounds¹¹. A striking feature of this stage, the relative lack of abnormal physical findings in the face of severe abdominal pain, is helpful in differential diagnosis⁶, and if recog-

nized, permits early surgical intervention while the bowel is still viable.

If permitted to continue, intestinal ischemia progresses to full-thickness infarction, and peritonitis develops. This stage is characterized by abdominal distension, direct and rebound tenderness and absence of bowel sounds, together with fever, leukocytosis and tachycardia^{11,16}. Serum amylase may be normal or elevated^{13,16}. Abdominal paracentesis, yielding a reddish-brown fluid with a fecal odor, confirms the diagnosis³. The final stage is characterized by shock, associated with release of endotoxin from the infarcted bowel⁶.

Fluid sequestration results in hypovolemia and hemoconcentration, which is manifested by a rise in hematocrit. Hemoconcentration with hematocrit over 50% was seen in 61% of patients with acute intestinal infarction in a series reported by Liavag. Roentgenographic findings in the early stages include nonspecific signs on the abdominal film such as absence of gas in the abdomen, a pattern of small bowel obstruction, or the splenic flexure sign. Findings suggesting bowel wall injury include thickening of the bowel wall with obliteration of the valvulae conniventes and narrowing of the lumen¹⁷. At a later stage, the presence of a cleft-like distribution of air in the bowel wall and of air in the portal venous system (Figures 1-3) is virtually diagnostic of intestinal infarction¹⁸. A barium study may reveal rounded projections into the lumen caused by edema and submucosal hemorrhage, the "thumbprint" effect¹⁶.

Angiography, including aortography and selective mesenteric arteriography, is the most specific diagnostic procedure in occlusive intestinal infarction¹⁶, though the distinction between thrombosis and embolism is often difficult¹⁷.

Non-Occlusive Infarction. In a significant percentage of cases of intesti-

MESENTERIC VASCULAR DISEASE

MUNIAGURRIA AND SYBERT

nal infarction (49% in the series of Ottinger and Austen¹³), no gross arterial or venous occlusion can be found at surgery or autopsy. A common feature in those cases is a sustained impairment in cardiac output, usually in the setting of myocardial infarction, septicemia or profound hypovolemia¹. In one series of 31 patients with non-occlusive infarction, 17 were in shock and 20 were in severe cardiac failure¹⁹. It is postulated that intestinal infarction in this setting results from sustained reflex splanchnic vasoconstriction, which reduces splanchnic blood flow below a certain critical level, resulting in functional occlusion¹. The clinical findings are similar to those of thrombosis or embolism, but certain angiographic features^{12,17}, as well as the clinical setting, may suggest this entity.

Inferior Mesenteric Artery Occlusion. In most patients, the inferior mesenteric artery may be ligated during surgery without resulting in colonic infarction². Isolated infarction of the left hemicolon occurs due to occlusion of the inferior mesenteric artery in the absence of adequate anastomoses with the superior mesenteric artery²⁰. Clinical features include abdominal pain and tenderness, predominantly in the left lower quadrant, and diarrhea, which is bloody in half the patients²⁰. Sigmoidoscopy may

reveal mucosal ulceration and gangrene. Barium enema often demonstrates spasm of the colon²⁰ and thumbprinting²¹. Once infarction occurs, the clinical picture resembles that of superior mesenteric artery occlusion, with peritonitis and shock. The course is quite variable, and patients who survive may present later with colonic obstruction secondary to stenosis².

Mesenteric Venous Thrombosis. Factors predisposing to mesenteric venous thrombosis include intra-abdominal infections, coagulopathies, polycythemia vera, portal hypertension, and trauma²². Oral contraceptives have been associated²³. In a recent series²², 32% of patients had a history of peripheral thrombophlebitis. In a significant percentage of cases no predisposing factor can be identified.

The clinical manifestations are more insidious in onset than in arterial occlusion¹⁶. Vague abdominal distress with intermittent colicky pain may persist for several days, accompanied by mild distention and vomiting²⁴. Later, with bowel infarction, the clinical picture cannot be differentiated from that of arterial occlusion²⁴.

Therapy. The treatment of acute intestinal infarction consists of immediate resuscitative measures, including fluid and blood replacement, anti-

biotics and nasogastric suction¹⁴, followed by surgery, which may include thromboemblectomy or bypass grafting in appropriate cases, as well as resection of nonviable segments of bowel. Because of the difficulty in assessing the viability of bowel during surgery, many authors recommend that bowel of questionable viability be left intact and re-examined 24 to 36 hours later at a second operation¹.

Several studies have suggested the value of postoperative anticoagulation in cases of mesenteric venous thrombosis²².

The use of dextran, massive doses of corticosteroids, continuous epidural anesthesia, and intra-arterial phenoxybenzamine has been recommended in treating intestinal infarction⁶, but their role remains unclear.

The overall mortality in mesenteric infarction has been estimated at 75% by Friedman and Sloan³. Liavag¹⁴ cites a figure of 90%, and attributes it in part to a delay in diagnosis.

Conclusions

Mesenteric vascular disease should be included in the differential diagnosis of all cases of abdominal pain of obscure etiology, especially in the setting of diffuse arteriosclerosis, myocardial infarction or hypoperfusion states. An early diagnosis made

on the basis of clinical features and arteriography permits earlier surgical intervention and may reduce the overall mortality.

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References

1. WILLIAMS, L. F., WITTENBERG, J., GRIMES, E. T., BYRNE, J. J.: Ischemic Diseases of the Bowel I. Ischemia of the Small Bowel. *Dis. Colon Rectum*, 1970, 13, 275.
2. WILLIAMS, L. F.: Vascular Insufficiency of the Bowel. *Disease-a-Month*, August, 1970.
3. FRIEDMAN, G., SLOAN, W. C.: Ischemic Enteropathy. *Surg. Clin. N. Amer.*, 1972, 52, 1001.
4. MIKKELSEN, W. P.: Intestinal Angina: Its Surgical Significance. *Am. J. Surg.*, 1957, 94, 262.
5. WOLMA, F. J., ALLUMS, J. A.: Mesenteric Artery Occlusion. *Texas Medicine*, 1970, 66, 64.
6. LEVINE, M. A.: Mesenteric Vascular Disease. *Geriatrics*, 1972, 27, 77.
7. LORD, R. S. A., STONEY, R. J., WYLIE, E. J.: Coeliac-axis Compression. *Lancet*, 1968, 2, 795.
8. HARJOLA, P. T., LATHIHARJU, A.: Celiac axis syndrome: Abdominal Angina Caused by External Compression of the Celiac Artery. *Am. J. Surg.*, 1968, 115, 864.
9. CARRON, D. B., DOUGLAS, A. P.: Steatorrhea in Vascular Insufficiency of the Small Intestine. *Quart. J. Med.*, 1965, 34, 331.
10. NUNN, D. B.: Chronic Intestinal Angina: A Report of Two Patients Treated Successfully by Operation. *Ann. Surg.*, 1972, 175, 523.
11. JACKSON, B. B.: Occlusion of the Superior Mesenteric Artery. Springfield, Ill., Thomas, 1963.
12. BRITT, L. G., CHEEK, R. C.: Non-occlusive Mesenteric Vascular Disease: Clinical and Experimental Observations. *Ann. Surg.*, 1969, 169, 704.
13. OTTINGER, L. W., AUSTEN, W. G.: A Study of 136 Patients with Mesenteric Infarction. *Surg. Gynecol. Obstet.*, 1967, 124, 251.
14. LIAVAG, I.: Diagnosis and Treatment of Acute Mesenteric Vascular Insufficiency. *Geriatrics*, 1969, 24, 49.
15. PIERCE, G. E., BROCKENBROUGH, E. C.: The Spectrum of Mesenteric Infarction. *Am. J. Surg.*, 1970, 119, 233.
16. PRICE, W. E., ROHRER, G. V., JACOBSON, E. D.: Mesenteric Vascular Diseases (editorial). *Gastroenterology*, 1969, 57, 599.
17. WITTENBERG, J., ATHANASOULIS, C. A., SHAPIRO, J. H., WILLIAMS, L. F.: A Radiological Approach to the Patient with Acute, Extensive Bowel Ischemia. *Radiology*, 1973, 106, 13.
18. WITTENBERG, J.: Ischemic Disease of the Bowel IV. Roentgenographic Findings. *Dis. Colon Rectum*, 1970, 13, 294.
19. MUSA, B. U.: Intestinal Infarction without Mesenteric Vascular Occlusion. A Report of 31 Cases. *Ann. Int. Med.*, 1965, 63, 783.
20. GIBSON, W. E., PEARCE, C. W., CREECH, O.: Infarction of the Left Hemicoln Due to Primary Vascular Occlusion. *Dis. Colon Rectum*, 1969, 12, 323.
21. BENTLIF, P. S.: Ischemic Disease of the Colon. *Southern Med. J.*, 1969, 62, 1452.
22. MATHEWS, J. E., WHITE, R. R.: Primary Mesenteric Venous Occlusive Disease. *Am. J. Surg.*, 1971, 122, 579.
23. CIVETTA, J. M., KOLODNY, M.: Mesenteric Venous Thrombosis Associated with Oral Contraceptives. *Gastroenterology*, 1970, 58, 713.
24. INAHARA, T.: Acute Superior Mesenteric Venous Thrombosis: Treatment by Thrombectomy. *Ann. Surg.*, 1971, 174, 956.

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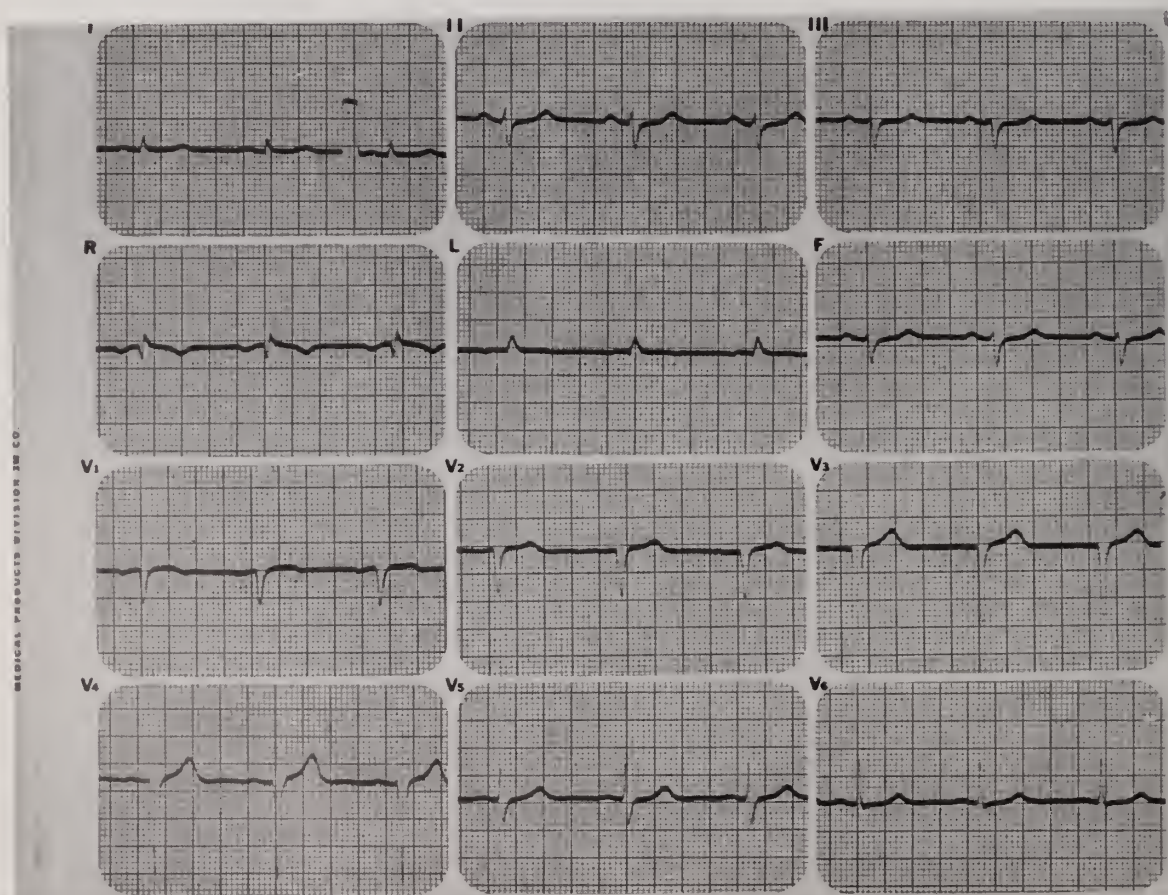
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ECG PROBLEMS

HISTORY: A 65-year-old man presenting himself for complete physical examination with no symptoms whatever referable to the cardiovascular system. Searching history fails to uncover any illness which might have represented acute myocardial infarction.

(for diagnosis see page 335)



Surgical (and Medical) Sequelae of Drug Addiction

GLENN W. GEELHOED, M.D.

Abstract

Over three hundred patients were seen in a four year period for the surgical complications of drug addiction in an urban population of 756,000 people containing an estimated 20,000 narcotic addicts. The surgical complications were largely due to techniques of administration and adulterants administered in "mainlining" and "skin-popping" using cut narcotic substances with septic and inflammatory reactions. In the extremities the venous and arterial inflammations were seen from intravascular administrations of contaminated narcotic, and fasciitis and multiloculated abscesses were seen from "skin-popping" or missed intravenous injections attempts. Right-sided endocarditis was seen in eight patients of whom six recovered. Pulmonary complications ranged from pulmonary edema, hilar lymphadenopathy, septic pulmonary emboli, and pulmonary infections each with peculiarities resulting from the addict's habits. Left-sided endocarditis was seen in five patients, only two of whom survived. Gastro-intestinal complications of drug addiction are predominantly medical rather than surgical; hepatitis is the most frequent gastro-intestinal complication of drug addiction with pseudo-intestinal obstruction and allegations of pancreatitis requiring careful diagnosis to avoid the laparotomy and narcotic

administration often sought by addicts with these symptoms.

With the spreading epidemic of drug abuse, surgeons should become increasingly aware of and familiar with the surgical complications of this psychosocial disorder and its many medical implications.

Drug abuse is an endemic disease in major American metropolitan areas which has spread through the suburbs and across socio-economic strata. Within the District of Columbia, a city of 756,000 population, there are an

Complications of drug addiction which will be brought to the surgeon's attention are largely due to the techniques of administration of the drug and other foreign material that is injected along with it, rather than to the drug itself.

estimated 20,000 narcotic addicts.¹ During a four year period, over 300 patients drawn from this population have been treated at the George Washington University Medical Center and affiliated hospitals for surgical problems resulting directly from their drug addiction. Excluded from detailed comment, but also noteworthy, are the indirect surgical sequelae of the addict's habits: these include trauma, resulting from inappropriate use of

machinery and locomotion while under the influence of drugs; the penetrating and blunt wounds of violence frequently encountered in the criminal support of the addict's habits; and reported "crush injury" of the extremities seen in lethargic addicts who are found after prolonged lying in positions that cause limb ischemia while they are comatose².

Complications of direct drug effect are infrequent in the afflicted addict, such as the pharmacology of the central nervous system depressant action of most narcotic drugs, and these tend to be managed medically. [Complications of drug addiction which will be brought to the surgeon's attention are largely due to the techniques of administration of the drug and other foreign material that is injected along with it, rather than to the drug itself.] The addict must instill an unknown substance via a variety of techniques and routes of administration in order to obtain some of the narcotic active ingredient effect that he seeks; the majority of the unknown substance he injects is adulterant. Associated with his notoriously poor techniques of administration and carried with the diluent are the infections and foreign reactive agents that give rise to the majority of surgical complications of addiction.

An outline of the surgical complications of drug abuse might be traced by following the circulation of the ad-

SURGICAL AND MEDICAL SEQUELAE OF DRUG ADDICTION

GEELHOED

TABLE 1

Surgical Complications of Drug Abuse by Injection

- I. Extremities
 - A. Peripheral venous
 1. Thrombophlebitis
 2. The puffy hand syndrome
 - B. Arterial
 1. Peripheral arteritis and transient ischemia
 2. Mycotic aneurysms of extremities
 3. Peripheral microembolization
 - C. Soft Tissue
 1. Necrotizing fasciitis
 2. Septic arthritis and myositis
 3. Multiloculated soft tissue abscesses
- II. Right-Sided Cardiac Complications
 - A. Tricuspid valvulitis and endocarditis
 - B. Pulmonic valvulitis and endocarditis
- III. Pulmonary Complications
 - A. Pulmonary edema
 - B. Hilar adenopathy
 - C. Septic pulmonary emboli
 - D. Pulmonary infections
 1. Aspiration pneumonia
 2. Bacterial pneumonia
 3. Tuberculosis
- IV. Left-Sided Cardiac Complications
 - A. Mitral valvulitis, endocarditis and systemic septic embolization
 - B. Aortic valvulitis, endocarditis and systemic septic embolization
- V. Gastro-Intestinal Complications
 - A. Pseudo-intestinal obstruction
 - B. Pseudo-pancreatic and biliary disease

dict's injection as it is expressed by its inflammatory reactions. (Table 1)

Extremities

Venous Complications

The antecubital fossa is the preferred site of self-administration of most intravenous drugs. The easily accessible cephalic and basilic venous systems become sclerotic, however, after repeated episodes of phlebitis and are no longer useful as a "main-line" to the cardiovascular system. Smaller and more distal veins are progressively searched out by the long-term addict. The veins of the hand are especially accessible, particularly for administration on the non-dominant side. These more peripheral veins have less adventitial support and extravasation of the injected substance occurs easily with resultant deep space infections spreading under the fascial compartments of the hand. With successive obliteration of the venous return from the hand and the scarring induced by repeated injections of inflammatory substances, the "puffy hand" syndrome³ results, secondary to both superficial venous and chronic lymphatic obstructions⁴. The gross appearance of the hand is seen in Figure 1. Reconstitution of the venous drainage from the hand is not possible. Fasciotomy may be necessary acutely and subsequent treatment usually consists of elevation of the affected extremity and systemic heparin and antibiotic administration. Twenty-two patients with the "puffy hand" syndrome were seen during the period covered by this series and 18 of these individuals required heparin therapy for slow and incomplete resolution of this complication.

Peripheral Arteritis

With progressive obliteration of venous injection sites, the addict may



FIG. 1. The "Puffy Hand Syndrome" seen in drug addicts secondary to both superficial venous and chronic lymphatic obstructions.

turn to intra-arterial injection either because the artery remains as a palpably localizable access to the circulation when no veins are accessible, or for the special sensation known as a "flash" or "hand trip" that results from intra-arterial injection. A "hit" in the brachial or radial artery causes a burning paresthesia throughout the arterial distribution and a hyperemic flush followed by a spasm of the artery with consequent ischemic symptoms. The peripheral pulse can be absent or diminished. Arteriography may demonstrate small vessel occlusion or spasm in the distribution of the larger arterial tree in the extremity above the injection site which appears uninvolved. (See Figure 2) Of four patients who were seen following intra-arterial injection, all were treated by intravenous heparinization and repeated intra-arterial injections of vasodilators during the period of acute spasm. Stellate ganglion block was attempted in one patient without relief.

The vascular lesion in a "hand trip" has several causes. Intimal damage secondary to the drug with necrosis of the arterial wall has been thought to give rise to thrombus propagation in the arterial tree. Extreme vasoconstriction has also been postulated secondary to catecholamine release from the injured artery. Microembolization of the small vessels with the particulate debris used as diluent for the narcotics is also thought to be likely in a number of cases of intra-arterial injection. In one of the patients treated in our series partial amputation of two digits was required while two others lost partial thickness of skin and subcutaneous tissue over the digits. Fasciotomy was required in the remaining patient to relieve the swelling and muscle spasm, but he nonetheless developed a subsequent Volkmann's contracture following the ischemia resulting from his intraarterial narcotic injection.



FIG. 2. Angiographic appearance of a drug addict's extremity following intra-arterial injection of drug and excipients demonstrating small vessel spasm and occlusion.

Mycotic Aneurysm

Repeated arterial puncture, particularly when the arterial puncture is done with septic technique and the instillation of inflammatory agents, can lead to mycotic aneurysm forma-

tion. These usually occur in narcotic addicts at the sites where the large extremity arteries are accessible, as in the antecubital fossae and the groin. Three patients in the present series developed mycotic aneurysms, and two had brachial arterial aneurysms

SURGICAL AND MEDICAL SEQUELAE OF DRUG ADDICTION

GEELHOED



FIG. 3. Mycotic aneurysm at the site of brachial intra-arterial injections.



FIG. 4. Necrotizing fasciitis in the extremity of an addict treated by sub-fascial catheter irrigations.

excised. Figure 3 illustrates one of these brachial artery aneurysms which appeared at the site of multiple intra-arterial drug injections. The third had a mycotic aneurysm in the femoral artery with an extensive area of sepsis around the femoral vessels. All three patients had resection of their mycotic aneurysms and bypass of the resected areas with successful bovine artery heterografts.

Septic Arthritis and Myositis

"Skin popping" is resorted to by some addicts who wish to inject narcotics subcutaneously when direct vascular route from "mainlining" is either not available or has been missed. The depot of narcotic and adulterant injection often becomes the site of local inflammation, either by the infective or irritant nature of the injected drug and excipient. The most frequent sites of arthritis and myositis, therefore, are the areas around the antecubital fossae or in the hands where venopuncture may have been attempted and missed. This complication can proceed to the next more frequently seen complication in the extremities of addicts, necrotizing fasciitis.

Necrotizing Fasciitis

Fourteen patients in the present series were afflicted with necrotizing fasciitis, in which the fascia containing the muscular and neurovascular compartments of the extremities liquified following sub-fascial injections of the narcotic and its inflammatory diluents (See Figure 4). The treatment of choice for patients with such a necrotizing fasciitis has been extensive drainage with catheter placement beneath the necrotizing fascia and regular irrigation through this drainage catheter.

Multiloculated Abscesses in the Extremities and Other Injection Sites

Injection site and metastatic abscess formation have been the single most frequently seen complication in the extremities of narcotic addicts who use various injection techniques. Seventy-one individuals were seen with multiloculated abscesses which required incision and drainage in various sites in the extremities (See Figure 5). Many of these abscesses grow staphylococcal organisms, but others show anaerobic flora. It is of particular interest that abscesses on the East Coast of the United States have been reported to grow clostridial organisms—tetanus in particular—a complication not reported on the West Coast. The explanation for this is thought to be in the diluent with which the heroin is cut on the street. The heroin merchandizers of the East Coast use quinine to "cut" the heroin in each bag, because quinine has a similar appearance, consistency, and bitter taste and mixes well with the heroin in the melting spoon prior to bulb syringe injection. One of quinine's properties is that it has a high redox potential and, injected into the extremity, creates appropriate conditions for anaerobic growth. The clostridial organisms carried in the primitive and unhygienic mainliner's kit, therefore, are facilitated in their growth by virtue of the quinine added to the intramuscular medium.

Cardiac Right Sided Cardiac Complications

Acute and sub-acute endocarditis following contaminated intravascular injection is a well known complication in drug addicts. The right sided endocarditis is distinctive enough to be considered separately, since the right side of the heart receives the full undiluted effect of the peripheral intravenous contamination. Endocardi-

tis can affect a previously normal tricuspid valve whereas pulmonic valve involvement is rare. *Staphylococcus aureus* is the predominant organism, and signs of this valvular heart disease are difficult to diagnose. The chief diagnostic clue to the presence of tricuspid valve endocarditis consists of multiple pulmonary infarcts without an identified source elsewhere in the peripheral venous system. Tricuspid valvulitis is extremely rare in the non-addict⁵. The most highly suggestive constellation of clinical findings leading to the diagnosis of tricuspid endocarditis is heroin addiction, positive blood cultures, and septic pulmonary infarction.

In a previously reported series of twenty-five patients with right sided bacterial endocarditis, twenty-three were heroin addicts⁶. The predominant clinical manifestations were related to septic pulmonary embolism in that series. Antibiotics were effective

in controlling infections due to gram positive cocci; however, if *Pseudomonas aeruginosa* was the etiologic agent in right sided endocarditis, it was resistant to therapy with antibiotics alone and excision of the infected tricuspid and/or pulmonary valves was necessary. Nine out of ten patients were cured of their endocarditis after excision of their infected tricuspid and/or pulmonary valves without prosthetic replacement, and the long-term survivors reportedly showed few significant hemodynamic difficulties. Another series⁷ suggested that there are ill effects of valve excisions without replacement, and that a prosthesis should be placed after septicemia clears. In the series reported by Arboula⁶, it was emphasized that antibiotic therapy should be attempted for six weeks or less, because if infection persisted beyond this period the endocarditis might spread to the left side of the heart where valve excision without replacement would be impossible.



FIG. 5. Multiloculated abscesses near injection sites requiring incision and drainage.

SURGICAL AND MEDICAL SEQUELAE OF DRUG ADDICTION

GEELHOED

TABLE 2

Right-Sided
Endocarditis in Narcotic Users*

Patient's	Age	Physical Findings	Organism	Treatment	Outcome
1.	28	Pericardial friction rub petechial hemorrhages	<i>S. aureus</i>	Cephalothin	Died
2.	31	Pericardial friction rub	<i>S. aureus</i>	Cephalothin, methicillin	Died, also developed hepatitis
3.	38	Soft apical murmur	<i>S. aureus</i>	Penicillin	Recovered
4.	22	Pleural friction rub	<i>S. aureus</i>	Penicillin, methicillin	Recovered
5.	49	Congestive heart failure	<i>S. aureus</i> & <i>S. albus</i>	Oxacillin, cardiac catheterization, valve replacement	Died; developed lung abscess, empyema, & sepsis
6.	38	Grade III systolic murmur, congestive heart failure	<i>S. aureus</i>	Penicillin, methicillin, cardiac catheterization, valve replacement	Recovered
7.	44	Grade III systolic murmur, congestive heart failure	<i>S. aureus</i>	Penicillin, cardiac catheterization, valve replacement	Recovered
8.	20	Grade III systolic murmur, congestive heart failure	<i>S. aureus</i>	Keflin, valvectomy	Recovered

* Tricuspid valve involvement and septic pulmonary emboli in each patient

In the present series, eight patients had right sided endocarditis involving the tricuspid valve (Table 2). Although only three patients had a cardiac murmur, each of them had clinical and radiologic evidence of multiple pulmonary septic emboli. *Staphylococcus aureus* was the infective organism in each. Three of the eight individuals with antibiotic-resistant endocarditis underwent cardiac catheterization and excision of the tricuspid valve with prosthetic replacement. One additional individual had tricuspid valvectomy without valve replacement, and is doing well eighteen months following operation. Two of the three patients

who underwent valve replacement survived and two of the four remaining addicts with tricuspid endocarditis treated with antibiotics alone survived.

Pulmonary Complications Pulmonary Edema

Acute pulmonary edema in heroin intoxication is a dramatic medical crisis and is usually severe leading to respiratory arrest if untreated. Pulmonary edema is the principal cause of death among narcotic addicts in New York City⁸. Nineteen patients in the present series were seen after intravenous drug injection with a history

of unconsciousness for a variable period. Upon returning to consciousness, these patients developed apprehension, dyspnea, cyanosis, and widespread rales with productive coughs yielding frothy sputum. The venous distension, hepatomegaly and gallop rhythm seen with the pulmonary edema of congestive heart failure were absent, although tachycardia was frequently present. Fluffy bilateral pulmonary infiltrates were visible on chest x-ray usually without cardiomegaly (Figure 6). Intensive medical treatment of the pulmonary edema was successful in twelve of the nineteen patients, whereas five experienced respiratory arrest while in the emergency room and could not be resuscitated. Two of the remaining patients died within three days of hospitalization from intractable pulmonary edema which led to pneumonia and pulmonary hemorrhage with sepsis. The precise mechanism of pulmonary edema in heroin addiction is unknown although the exudative pneumonitis seen in opiate addicts and first described by Osler⁹, resembles fulminant influenzal bronchopneumonia. The pulmonary edema of narcotic addiction responds to the empiric methods of management of pulmonary edema in general, despite our lack of specific information as to the pathogenesis of this disorder.

Hilar Lymphadenopathy

Hilar lymphadenopathy is one of the most common features of the narcotic addict's chest x-ray. The hilar adenopathy results from the continuing impaction of a great deal of foreign debris injected by the addict along with the small quantity of heroin he hopes to receive in each bag purchased. Over 95% of the average street-purchased heroin consists of diluent made up of a variety of excipient powders including quinine, sugars, talc, starch, and other fillers that are

chosen for their resemblance to the heroin powder, not with regard to their beneficial effects on the lung. These impurities continually injected into the right heart circulation are filtered by the pulmonary lymphatics where much of the debris is captured by the reticuloendothelial system. Chest x-rays and post-mortem examinations performed on addicts reveal generalized hyperplasia of the entire lymphatic system, but especially the lymph nodes at the hilum of the lung and liver. Although the chronic delivery of this antigen mass may stimulate the reticuloendothelial system, chronic narcotism is known to inhibit phagocytosis and lymphocyte mediated immunity¹⁰. Therefore, although the morphologic features of the lymphatic system are stimulated to hyperplasia by chronic narcotics injections, the functional capacity of these enlarged lymph nodes is probably diminished.

Twenty-three patients with known chronic drug abuse in this series had asymptomatic pulmonary hilar lymphadenopathy in the absence of active pulmonary parenchymal disease. Sixteen of these patients had some evidence of generalized lymphadenopathy to go along with their hilar lymphadenopathy. Mediastinoscopy and node biopsy were performed in ten patients to rule out sarcoid, tuberculosis or lymphoma, and histologic examination of these nodes showed nonspecific lymphocytic hyperplasia. Two of these patients, who came to postmortem examination following death from other causes, were found to have multiple talc granulomas noted in the lungs.

Septic Pulmonary Emboli

Septic foci in the venous circulation from the peripheral venous injection sites to the pulmonic valve may give rise to septic pulmonary emboli. The multiple septic complications of con-

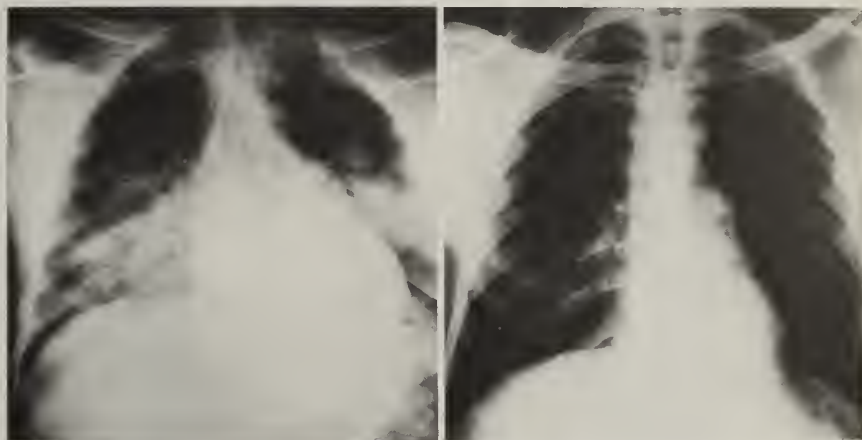


FIG. 6. Radiographic appearance of pulmonary edema in the heroin addict.



FIG. 7. "Mainliner's Lung" as seen on chest x-ray showing multiple migratory pulmonary abscesses without evident endocarditis to account for septic embolization.

taminated injections in the extremities and secondary endocarditis in the right side have previously been discussed. Septic pulmonary emboli are common enough in drug addicts to give rise to the radiographic picture called "mainliner's lung" consisting of multiple bilateral pulmonary lesions.

Thirteen patients were treated in this series for single or recurrent septic pulmonary emboli without evident bacterial endocarditis underlying their embolic phenomena. Five of these thirteen patients had hemoptysis and pleuritic chest pain. The "mainliner's lung" appearance on chest x-ray (See Figure 7) was present in the majority

of these patients. Others presented the radiographic portrait of migratory lung abscesses with new pulmonary abscesses developing as previous ones were healing.

Seven patients grew coagulase-positive staphylococcus aureus on repeated blood cultures, and three others grew beta-hemolytic streptococcus group A. Blood cultures were sterile in the remaining three patients. Sputum cultures taken in these individuals were unrevealing, since the pulmonary abscesses originated from the hematogenous rather than airway routes. When pneumatization of these pulmonary abscesses occurred, re-

SURGICAL AND MEDICAL SEQUELAE OF DRUG ADDICTION

GEELHOED

TABLE 3

Left-Sided Endocarditis in Narcotic Users

Patient's Age	Physical Findings	Valve	Organism	Treatment	Outcome
1. 20	Basilar systolic murmur, cerebrovascular accident	Aortic	Enterococcus	Ampicillin	Recovered; had subsequent renal artery embolus
2. 26	Left sternal systolic murmur, recurrent peripheral emboli	Aortic	Candida parapsilosis	Amphotericin B, Prostaphlin	Died in renal failure, ? rheumatic heart disease
3. 28	Apical systolic murmur, pericardial friction rub, congestive heart failure	Mitral & tricuspid	Streptococcus viridans	Lincomycin, cardiac catheterization, mitral valve prosthesis, tricuspid annuloplasty	Recovered
4. 21	Systolic murmur, pericardial friction rub, congestive heart failure	Aortic & Mitral	Streptococcus viridans	Penicillin, streptomycin, cardiac catheterization, aortic and mitral prostheses	Died in recovery room
5. 40	Systolic & diastolic murmur, congestive heart failure, peripheral emboli	Aortic	Streptococcus viridans	Penicillin, cardiac catheterization, valve replacement	Died—valve incompetent

peated bronchoscopy and vigorous chest physical therapy were employed for drainage. Despite these measures and vigorous antibiotic treatment four patients required lobectomy for chronic lung abscesses.

Pulmonary Infections

In addition to the septic pulmonary emboli which delivers sepsis to the lung by the hematogenous route, the narcotic addict is also prone to pneumonitis by airway contamination. Narcotic addicts who have maintained their habit for any period of time are generally debilitated in terms of their nutrition and host resistance. The depressed cell mediated immunity seen in drug addicts may also be a mechanism whereby these patients are more susceptible to pulmonary infections.

Aspiration pneumonitis is a common sequel of narcotic addiction where overdose and resultant lethargy and respiratory depression give rise to anoxia, often associated with vomiting and aspiration of gastric contents. The roentgenographic findings are that of a right middle lobe or a lower lobe pneumonitis which may progress to

segmental atelectasis following bronchial obstruction. Treatment for aspiration pneumonitis in the narcotic addict involves awakening the patient with intravenous narcotic antagonists as well as prompt and repeated bronchoscopy and attention to bronchial toilet. When detected early, steroid therapy may be of benefit.

Aspiration pneumonitis or pulmonary edema resulting from intravenous heroin administration may lead to a superimposed bacterial infection. Narcotic addicts are much more susceptible to microbial pneumonia than is the normal population. Nine addicts were seen in this series complaining of fever and unproductive cough without explanatory sources of the fever in peripheral sepsis or right sided endocarditis. Chest x-ray examination revealed no septic emboli in this group but each had pneumonitis confined to one lobe with a hematologic picture of leukocytosis of between 12,000 and 25,000 cells per milliliter. Sputa from each patient demonstrated large numbers of polymorphonuclear leukocytes, with sputa positive for *Diplococcus pneumonia* in five patients and *Klebsiella pneumonia* and *Haemo-*

philus influenzae in one patient each. No organisms were found in the two remaining patients that could account for their pneumonitis. Two of these patients had developed their pneumonia secondary to aspiration and the remaining had all had previous upper respiratory tract infections. In addition to the decreased host resistance and tendency to aspiration as causes for the increased frequency of pneumonitis in these patients, the respiratory depression of narcotic addiction may lead to depressed sighing and coughing reflexes and also to alveolar hypoventilation which may predispose the patient to atelectasis. The inability to clear the airway of the bacteria that may settle there because of this respiratory depression may account for this increase in pneumonitis in drug addicts. One of the patients with pneumonitis proved to have tuberculosis. An increased incidence of tuberculosis among heroin addicts has been previously reported both clinically¹¹ and at postmortem examination¹²

Left-sided Endocarditis

Five patients in the narcotic addict



FIG. 8. An upright abdominal film in a narcotic addict with pseudo-intestinal obstruction.

population seen in this series had left-sided endocarditis. Three of these patients grew *Streptococcus* from their blood, and *Enterococcus* and *Candida* were found in one each of the remaining patients. Each of these patients showed systolic valvular murmurs in contrast to those with right-sided endocarditis. Each had had episodes of systemic emboli. Two of these five patients were treated by drug therapy only and one of these died from renal failure. The other survived and underwent embolectomy for a right renal artery embolus. Three patients underwent mitral valve replacement and tricuspid annuloplasty. Two of these three patients died following their valve replacements with continuing

sepsis and cardiac failure and the third patient recovered successfully (Table 3).

If the known drug addict develops endocarditis, it is likely to occur on the left side of the heart; this statement is true despite our previous statement that tricuspid valvulitis is rare except in addicts. Narcotic addicts may develop both right and left-sided endocarditis, and, as Arbulo noted⁶, the endocarditis usually spreads from the right side of the heart to the left. In several previously reported reviews the mortality rate in narcotic-induced endocarditis ranges from thirty-five to fifty percent. This high mortality is related to valve destruction which results in hemodynamic failure, to the

occurrence of emboli, and to septicemia in chronic addicts especially considering their usually debilitated condition. If left-sided valvular failure—particularly aortic valve destruction—occurs only prompt surgical intervention can salvage such a patient from intractable congestive failure before adequate antimicrobial therapy can be completed. Though aggressive left-sided valvular excision and prosthetic replacement can meet with successful outcome, the danger of subsequent infection of these prostheses is high, particularly when considering the low cure rate of the underlying drug addiction itself which will lead to recurrent septicemia circulating this time around prosthetic valves.

Gastrointestinal Complications Pseudo-Intestinal Obstruction

Twelve patients have been seen with pseudo-intestinal obstruction. These patients present with classic findings of bowel obstruction including distension, obstructive bowel sounds, and a radiographic picture showing dilated loops of bowel in which air fluid levels may be present. Many narcotic addicts have scarred abdomens from trauma, violence, and subterfuges worked upon previous surgeons in attempts to sustain their habit. It would be easy for the unwary surgeon to consider the much scarred abdomen and obstructive picture on x-ray diagnostic of mechanical bowel obstruction. The narcotic itself can render bowel motility abnormal and give rise to any of the findings of an ileus that may be mistaken for obstruction. Diagnosis of this condition depends on careful radiographic study of the abdomen in which certain signs of ileus may be detected. Figure 8 shows the upright abdominal film in a narcotic addict with pseudo-intestinal obstruction. Treatment is conservative electrolyte replacement and tube decompression.

SURGICAL AND MEDICAL SEQUELAE OF DRUG ADDICTION

GEELHOED

If cecal distension of twelve centimeters or more is apparent, operative intervention may be required to prevent perforation and to establish a diagnosis by exclusion.

Pancreatic or Biliary Disease

Hepatitis is an extremely frequent complication of drug addiction, and is probably the single most common cause for the medical admission of a narcotic addict. A common fallacy is that pancreatitis is also more frequent in the narcotic addict. Pancreatitis in the addict population may be a myth in that only two patients have been diagnosed in five years at the Narcotics Hospital in Lexington, Kentucky and review of their charts left doubt as to the accuracy of the diagnosis of pancreatitis in both^{1,3}. There is a surprising rarity of chronic alcoholism in narcotic addicts, which may account for the rarity of pancreatitis in this population of patients. Moreover, the jaundice that is so frequently a part of the past of narcotic addicts who have suffered hepatitis may be mistaken for obstructive jaundice in the patient who also gives a history of abdominal pain. Rather than assuming an obstructive etiology for the narcotic addict's crampy abdominal pain and jaundice, Eiseman states, "It is safe to assume that any confirmed addict has had hepatitis"^{1,3}. As previously noted, narcotic addicts do have lymphadenopathy, particularly around the hilum of the liver, and this may be associated with splenomegaly. Nonetheless, the mention of obstructive bowel lesions and biliary and pancreatic obstructive disease in the narcotic addict is largely to point out that these lesions are rather rare in this population, and the clever addict can use the constellation of symptoms based on his pseudo-obstructive disease to obtain narcotics or laparotomy from the unwary surgeon.

References

1. DUPONT, ROBERT L., PIEMME, THOMAS E.: Estimation of the number of narcotic addicts in an urban area, *Medical Annals of the District of Columbia* 1973, 42:323.
2. SHREIBER, S. N., BERNSTEIN, L., LIEBOWITZ, M., SRINAVASAN: Crush syndrome in heroin-induced coma, Reported at American Academy of Orthopaedic Surgeons, Washington, D.C., 1972.
3. ABELES, H.: Puffy-hand sign of drug addiction *New England Journal of Medicine* 1965, 273:1167.
4. NEVIASER, R. J., BUTTERFIELD, W. C., WIECHE, D. R.: The puffy hand of drug addiction *J. Bone and Joint Surgery (Am.)* 1972, 54:629.
5. HURST, J. W.: Cardiac disease in drug abuse *Medical Complications of Drug Abuse*, AMA Communications Division, 1971.
6. ARBULU, A. KAFI, A., THOMS, N. W., WILSON, R. F.: Right sided bacterial endocarditis *Annals of Thoracic Surgery* 1973, 16:136.
7. MICHL, L., SHUMACKER, H. B. Jr., HOBBS, D.: Tricuspid valvectomy *Surg. Gynecology & Obst.* 1973, 137:590.
8. SIEGEL, H., HELPERN, M., EHRENREICH, T.: The diagnosis of death from intravenous narcotics *J. Forensic Science* 1966, 11:1.
9. OSLER, W.: Oedema of left lung-morphia poisoning *Montreal General Hospital Report* 1880, 1:291.
10. OH, J.: Experimental and clinical observations regarding chronic opium and the abstinence phenomena of opium addicts *Jap. J. Medical Science* 1938, 11:79.
11. SAPIRA, J. D.: The narcotic addict as a medical patient *Am. J. Med.* 1968, 45:555.
12. HELPERN, M., RHO, Y. M.: Deaths from narcotism in New York City: incidence, circumstances and post-mortem findings *N.Y. State J. Med.* 1966, 66:2391.
13. EISEMAN, B., LAM, R. C., RUSH, B.: Surgery on the narcotic addict *Annals of Surgery* 1964, 159:748.

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SPECIAL ARTICLE

PSRO, SSA and Private Practice of Medicine

RUSSELL D. SQUIRES, M.D. AND PAUL R. MOYER, M.D.

Introduction

Public Law 92-603 was signed into law by the President on October 30, 1972, as the Social Security Amendments of 1972. Section 249 (F) of P.L. 92-603, commonly known as the PSRO law, and Section 237 (c) of this law are of special interest to practicing physicians. These sections have made it possible for non-physician fiscal agents of the Federal government to intervene directly in the delivery of institutional medical care and services and hence to intervene indirectly in the practice of medicine.

An example of such intervention is contained in rules proposed by the Commissioner of Social Security of the Social Security Administration and published in the January 9, 1974 Federal Register. These proposed rules are intended to amend already existing regulations governing utilization review procedures for hospitals and skilled nursing homes as originally set forth in the Social Security Act and its subsequent amendments. In particular, attention is directed to page 1450, paragraph 4, of these proposed rules where the final decision regarding the need of a covered level of institutional medical care and services can become the function of a fiscal intermediary acting for the above mentioned agencies of the Federal government.

These proposed rules are clearly not in accord with the AMA policy as stated in the amended portion of

It is contended that these legal considerations of the proposed rules represent a real and present threat to the proper conduct of the patient-physician relationship, not a hypothetical threat.

Report EE as adopted by the House of Delegates of the AMA at its meeting in Anaheim, California with respect to third party intrusion into the practice of medicine. Furthermore, these rules have been proposed despite Section 1801 of Title XVIII (Medicare) of the Social Security Act which states the following:

Nothing in this title shall be construed to authorize any Federal officer or employee to exercise any supervision or control over the practice of medicine or the manner in which medical services are provided or over the selection, tenure or compensation of any officer or employee of any institution, agency, or person providing health services; or to exercise any supervision or control over the administration or operation of any such institution, agency or person.

Authority for proposing such rules is based on Section 237 (c) of P.L. 92-603 which amends Section 1861 (k) of the Social Security Act, 42 U.S.C. 1395x(k), by adding authority under which the Secretary of HEW may require that the utilization review procedures established under the Medicaid program (Title XIX of the Social Security Act) be substituted for the utilization review procedures for

the Medicare program (Title XVIII of the Social Security Act) should the Secretary of HEW determine that the utilization review procedures for Medicaid program be superior to those for Medicare. The authority for this substitution is clearly stated in the law. However, the Commissioner of Social Security, with the approval of the Secretary of HEW, applied different or additional requirements to the utilization review procedures for Medicaid before proposing that they be substituted for the utilization review procedures for Medicare, (see page 1448 of the January 9, 1974 Federal Register). The authority for making such different or additional requirements before substitution is not clearly stated in the law.

Another possible legal consideration is that Section 249 (F) of P.L. 92-603 and the proposed rules may be considered discriminatory on the part of the Federal government with respect to beneficiaries of Medicare and Medicaid. Fiscal intermediaries, therefore, in order to obviate this consideration and for reason of efficiency of administrative uniformity may extend any changes in regulation governing Section 249 (F) of P.L. 92-603 resulting from these proposed rules to include all beneficiaries.

It is contended that these legal considerations of the proposed rules represent a real and present threat to the proper conduct of the patient-physician relationship, not a hypothetical threat.

PSRO, SSA AND PRIVATE PRACTICE OF MEDICINE

SQUIRES AND MOYER

Apart from legal technicalities the essential issues are: (1) to what extent should a fiscal intermediary of any organization which indemnifies medical care and services be authorized to deny reimbursement to their beneficiaries for covered care and services as authorized by law and prescribed by the physician of the beneficiary? (2) who should become the defendant in a legal suit brought by the beneficiary for grievance allegedly resulting from such denials? (3) what effect will the prospect for such denials and their possible consequences have on the patient-physician relationship and the treatment of the patient and his illness? and (4) to what extent is it proper for the Federal government to regulate that which it subsidizes? The extent of such regulation should be considered separately with respect to fiscal and professional functions.

Important Provisions of Section 249 (F) of P.L. 92-603

One of the many interesting, if not disturbing, provisions of Section 249 (F) of P.L. 92-603 is that it leaves the door open for a variety of approaches to the progressive implementation of the requirements of this law. Another is that in most instances, final or penultimate decisions regarding the implementation of this law will be left to the discretion of the Secretary of HEW; at least short of additional action by the Congress or the courts. These aspects of P.L. 92-603 engender concern regarding future effects on the patient-physician relationship, as does the prospect of future additional intervention in the practice of medicine by the Federal government and its various third party representatives, such as fiscal intermediaries.

Background to the Enactment of P.L. 92-603

Section 249 (F) of P.L. 92-603

provides for the establishment of independent Professional Standards Review Organizations from which the law acquired its common name, the PSRO law. The establishment of independent PSROs was recommended by the Senate Finance Committee as a partial solution to what its members believed to be two major problems involving the delivery of medical care and services to citizens eligible for Medicare and Medicaid, namely, rising health care costs and a high incidence of medically inappropriate care and services. Although undisputable evidence for the latter belief was not presented, the Committee nevertheless felt that overutilization of care and services provided by Medicare and Medicaid was a significant factor in the increasing cost of such care and services. The program prior to October 30, 1972 already contained a number of utilization controls, but the Committee considered them inadequate. The Committee also cited what it believed to be a number of deficiencies in already existing SSA Regulation. Included amongst these deficiencies were lack of program coordination, lack of professional participation in support of review activities, restriction of required review to institutional care, and reviews which were only token in nature.

The Committee, therefore, proposed amendments to the Social Security Act which would provide for an independent review mechanism, through which practicing physicians could assume full responsibility for reviewing the utilization of professional medical care and services.

The Senate proposal was adopted by the House/Senate conferees with three major modifications: (1) required review was restricted to institutional care; (2) prior to January 1, 1976, only physician-sponsored organizations could serve as PSROs; and (3) provision was made for a referendum to determine if an organization

requesting to serve as a PSRO prior to January 1, 1976, was substantially representative of all practicing physicians.

Intention of, and Motivation for, Enactment of Section 249 (F) of P.L. 92-603

The avowed intent of Section 249 (F) of P.L. 92-603, therefore, is to reinforce the medical profession's activities which are directed toward improving the independent professional medical utilization review of the necessity, of the proper quality, and of the appropriateness of the level and duration of institutional medical care and services which are subsidized by the Federal government and are made available to eligible citizens by Medicare and Medicaid. The alleged motivation for the enactment of this section of the law stems from Congressional concern for the accelerating rate of rise in costs of federal subsidy of institutional medical care and services. Advocates of this section of this law feel that its implementation and enforcement will have a favorable effect not only on the quality and utilization of institutional medical care and services, but also on the rising cost of institutional medical care and services. Section 249 (F) of P.L. 92-603, however, does not make provisions for setting of fees and reasonable charges to be collected by providers of institutional medical care and services, or for the validation of claims for reimbursement for authorized medical care and services: that is, the method of payment to be made by the providers of institutional medical care and services rendered to the citizens eligible for Medicare and Medicaid. These functions had been already assigned to the Social Security Administration Bureau of Health Insurance for Medicare and the Social and Rehabilitation Services' Medical Services Administration for Medicaid. These agencies are directly

accountable to the Secretary of HEW, not indirectly accountable to the Secretary of HEW via the Assistant Secretary for Health and Scientific Affairs as are the PSROs. Fiscal intermediaries acting for these agencies usually negotiate contracts with the provider institutions, such as hospitals, regarding the reasonableness of charges and the validity of claims for authorized institutional medical care and services rendered to citizens eligible for Medicare and Medicaid.

Functions of PSROs and Fiscal Intermediaries

It would appear that in making use of the provisions of Sections 237 (c) and 249 (F) of P.L. 92-603, the Social Security Administrator has unfortunately and improperly attempted to assign to fiscal intermediaries professional medical utilization review functions which are intended to be the authorized functions of independent PSROs. It was intended that such agencies or their fiscal intermediaries, which were authorized the task of validating claims reimbursement, should exercise the responsibility of assuring Congress that public funds are not used to reimburse charges for institutional medical care and services which are not authorized by the law governing Medicare and Medicaid. It was not intended that Federal agencies or their fiscal intermediaries authorize the task of administering claims reimbursement should also be responsible for assuring Congress of the necessity, of the proper quality and of the appropriateness of the level and duration of professional institutional medical care in whole or in part. It was intended that assurance of the necessity, of the proper quality and of the appropriateness of the level and duration of professional medical services be provided to Congress, if and when necessary, as prescribed by law, only by practicing physicians operating di-

rectly through the Office of PSRO-NOT, for example, THROUGH SSA TO CONGRESS, or OFFICE OF PSRO VIA SSA TO CONGRESS. All that should be provided to agencies authorized the task of administering claims reimbursement or their fiscal intermediaries, is the identification of the patient and an itemized list of the specific types of medical care and services rendered to that patient. No other information or assurance should or need be supplied by the patient or providers to such agencies or their fiscal intermediaries authorized the task of administering claims reimbursement.

Confusion Regarding Functions of PSROs and Fiscal Intermediaries

This unfortunate and improper attempt to assign professional medical utilization review functions to fiscal intermediaries of Federal agencies is doubtlessly in part due to confusion regarding the alleged motivation for the enactment of P.L. 92-603 mentioned earlier, and the avowed intent of this law.

Early in 1973 the Office of Management and Budget allegedly set out to somehow find a way to restrain the accelerating rate of rise of expenditure of public funds for federally subsidized health care. After failing to obtain enactment of legislative measures which would have required beneficiaries to pay a larger share of their hospital bills through increased deductibles and copayments, the OMB persuaded the Social Security Administration to suggest a cost-saving proposal. Apparently without obtaining undisputable data to support the validity of their suggestion, the SSA not only anticipated the advent of PSROs but also proposed the use of an optional review mechanism provided in Section 1155 (2) of P.L. 92-603, that is, preadmission certification, an authorized function of PSROs-to

thereby curtail admission of patients eligible for Medicare and Medicaid to hospitals and skilled nursing homes. Furthermore, SSA indicated that such review was to be implemented and enforced by fiscal intermediaries who were authorized to manage Federal agencies charged with reimbursement of authorized institutional medical care and services to beneficiaries of Medicare and Medicaid. Subsequently, SSA has already attempted on at least two occasions to propose rules which will infringe upon or usurp the authorized independent professional medical review prerogatives and functions of PSROs, such as preadmission certification review. An attempt in May, 1973 was at least temporarily forestalled. If the current attempt to propose rules to amend institutional utilization review procedures, published in the January 9, 1974 Federal Register, is not also successfully forestalled, these proposed rules will become effective regulations and fiscal intermediaries will usurp PSRO functions.

Small comfort may be taken from the possible temporary nature of the above mentioned proposed SSA rules. It is conceivable that some or all of such proposed rules, if they ultimately become regulations, may be revoked by PSRO when Section 249 (F) of P.L. 92-603 becomes fully effective. Fully effective implementation of PSROs may not, according to this law, occur before January 1, 1976, during which time the SSA regulations will have become fully implemented. Furthermore, at the discretion of the Secretary of HEW, PSROs after January 1, 1976 are not necessarily required to include physicians in order to carry out their review functions. In fact, for example, after January 1, 1976 (see Section 249 (F) of P.L. 92-603) this law makes it possible for fiscal intermediaries to function both as fiscal agents of SSA as well as PSROs at the discretion of the Secretary of HEW. Therefore, it would

PSRO, SSA AND PRIVATE PRACTICE OF MEDICINE

SQUIRES AND MOYER

appear most likely that if the proposed SSA regulations go into effect, are implemented, staffed and enforced, the functions of the PSROs will have in fact been taken over by the fiscal intermediaries of the federal claims reimbursement agencies, and since they will already be fully operational, federal management for supposedly practical and expedient reasons will continue to permit fiscal intermediaries to perform both their assigned fiscal functions as well as professional medical utilization review functions. Thus, if and when PSROs come into being they will serve no critical function.

Should the Secretary of HEW fail to properly exercise his extensive authority for the implementation of Section 249 (F) of P.L. 92-603 without due regard to Section 1801 of Title XVIII (Medicare) of the Social Security Act as well as the recommendations of the Senate Finance Committee mentioned earlier, and should the Secretary of HEW continue to support attempts to deprive PSROs of part of all of their authorized functions of independent professional medical utilization review, a realistic consequence will be strong objections and continued aggressive attempts to circumvent by any legal means such rules and regulations by many practicing physicians. Therefore, before such proposed rules, as published in the January 9, 1974 Federal Register, are employed to effect changes in already existing relevant regulations, it is strongly recommended that, first, lines of communication and authority existing between the various Federal and private agencies involved in the administration of Medicare and Medicaid be clearly defined in terms of the intent of the existing law. Second, the intended separation of fiscal authority and professional medical utilization review authority must be clearly and properly defined and properly allocated. Independent professional medical utiliza-

tion review authority must be carried out entirely by practicing physicians and in no way be shared by Federal agencies assigned the task of reimbursement of charges (or their fiscal intermediaries). Third, the use of pre-admission certification review, which is an optional professional medical review function of independent PSROs, and of any other form of professional medical review function of independent PSROs must not be in any way a shared function of fiscal intermediaries. Exercise of all professional medical review functions should be left entirely to the discretion of the Office of PSROs for whatever reason they may choose to use such functions.

Since these comments were written, there has been published in the AMA News of February 11, 1974, information which indicates that the Secretary of HEW will, in whole or in part, "not pursue his controversial proposed regulations" as published in the January 9, 1974 Federal Register. Despite the encouraging nature of this information, it is far from clear as to whether or not the Secretary of HEW will formally withdraw all or part of the above mentioned proposed rules. Furthermore, should he withdraw the proposed rules, the essential issues raised and the recommendations suggested in these comments will remain essentially unchanged.

The primary issue is to what extent can Federal agencies modify existing regulations by proposing rules that apparently violate the intent of the law which the regulations are intended to implement? Such proposed rules published in the Federal Register will in effect become law if they remain unsuccessfully challenged. Such violations will continue to plague the practice of medicine unless formally and effectively challenged by any legal means by practicing physicians with the active support of organized medicine and their academic colleagues.

Dr. Squires, Professor of Clinical Engineering, George Washington University Medical Center, Washington, D.C. 20037.

Dr. Moyer, Assistant Professor of Clinical Engineering, George Washington University Medical Center, Washington, D.C. 20037.

Reprint requests may be addressed to Dr. Squires at the George Washington University Medical Center, Washington, D.C. 20037.

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can synthesize vitamin C**



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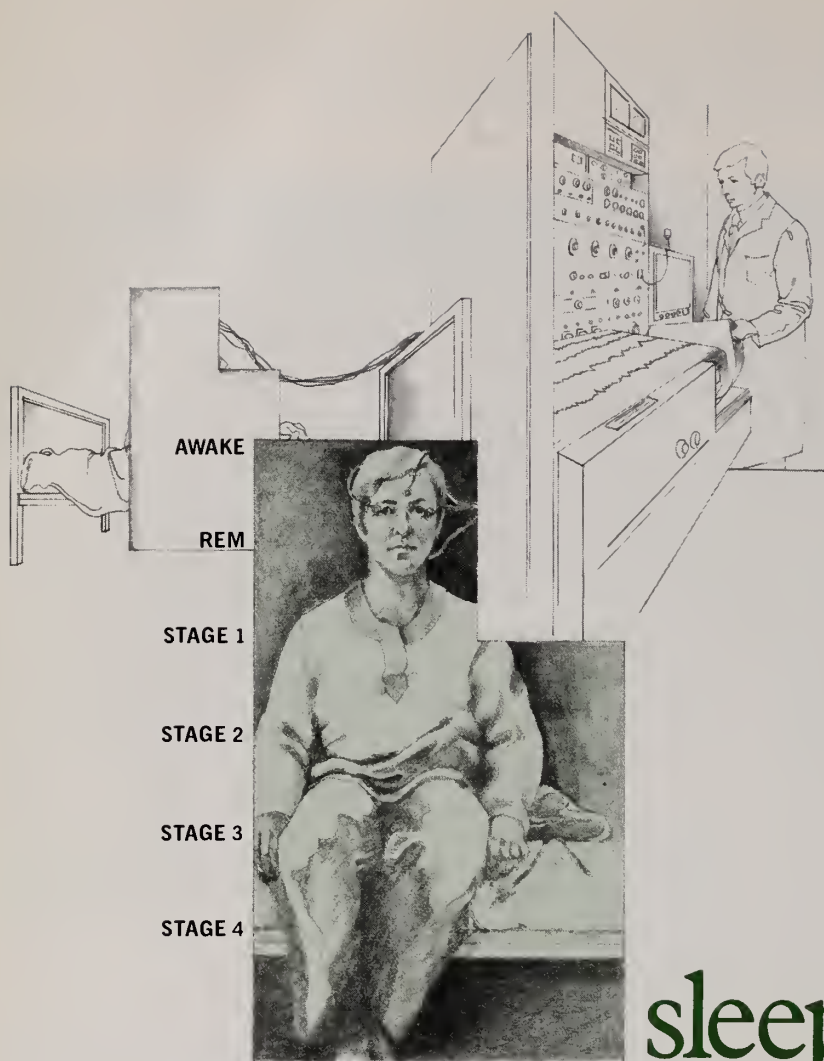
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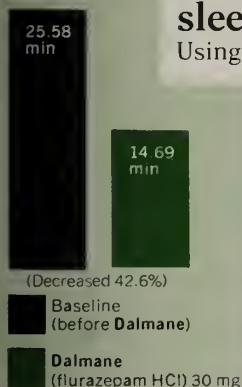


sleep
begins within
17 minutes, on average ...
an initial benefit of

Dalmane[®]
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22-night clinical study of insomnia patients
in the sleep research laboratory and at home¹

Three insomnia patients selected for difficulty falling asleep were administered Dalmane (flurazepam HCl) 30 mg for 14 consecutive nights. Placebo was given for four nights prior to and four nights after Dalmane. Physiologic tracings on Dalmane nights 1-3 showed sleep induction time averaged 13.90 minutes; on Dalmane nights 12-14, 18.80 minutes. Combined average for the 6 monitored drug nights was 16.35 minutes.¹

Average Time Required
to Fall Asleep (4 Studies,
16 Subjects²⁻⁵)



confirmed by clinical studies in four geographically separated sleep research laboratories²⁻⁵

Using a 14-night protocol involving eight insomniac and eight normal subjects, four studies confirmed the sleep-inducing effectiveness of Dalmane (flurazepam HCl) and the reproducibility of this response. On average, one 30-mg capsule induced sleep within 17 minutes. In all these studies, Dalmane induced sleep rapidly, reduced nighttime awakenings, and provided 7 to 8 hours of sleep without repeating dosage²⁻⁵

Dalmane (flurazepam HCl) induces and maintains sleep, with relative safety

Dalmane is generally well tolerated; morning "hang-over" has been relatively infrequent. While dizziness, drowsiness, lightheadedness and the like have been noted most often, particularly in the elderly and debilitated, physicians should be aware of the possibility of more serious reactions, as noted below.

Before prescribing Dalmane (flurazepam HCl), please consult Complete Product Information, summary of which follows:

Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening; in patients with recurring insomnia or poor sleeping habits; and in acute or chronic medical situations requiring restful sleep. Since insomnia is often transient and intermittent, prolonged administration is generally not necessary or recommended.

Contraindications: Known hypersensitivity to flurazepam HCl.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Use in women who are or may become pregnant only when potential benefits have been weighed against possible hazards. Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated, initial dosage should be limited to 15 mg to preclude oversedation, dizziness and/or ataxia. If combined with other drugs having hypnotic or CNS-depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with latent depression or suicidal tendencies. Periodic blood counts and liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported were headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins and alkaline phosphatase. Paradoxical reactions, e.g., excitement, stimulation and hyperactivity, have also been reported in rare instances.

Dosage: Individualize for maximum beneficial effect. *Adults:* 30 mg usual dosage; 15 mg may suffice in some patients. *Elderly or debilitated patients:* 15 mg initially until response is determined.

Supplied: Capsules containing 15 mg or 30 mg flurazepam HCl.

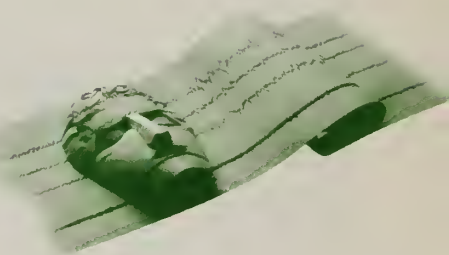
REFERENCES: 1. Kales A, et al: *Arch Gen Psychiatry* 23:226-232, Sep 1970

2. Karacan I, Williams RL, Smith JR: The sleep laboratory in the investigation of sleep and sleep disturbances. Scientific exhibit at the 124th annual meeting of the American Psychiatric Association, Washington DC, May 3-7, 1971

3. Frost JD Jr: Data on file, Medical Department, Hoffmann-La Roche Inc, Nutley NJ

4. Vogel GW: Data on file, Medical Department, Hoffmann-La Roche Inc, Nutley NJ

5. Dement WC: Data on file, Medical Department, Hoffmann-La Roche Inc, Nutley NJ



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One 15-mg capsule h.s. — initial dosage for
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- induces sleep within 17 minutes, on average
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Opinion & Dialogue

Is there a need for a drug compendium?

A drug compendium of the type I envisage would fill a definite need for the practicing physician. Such a compendium would give him all the information necessary for using

a drug intelligently, and it would do so in a clear, concise, convenient, objective and balanced fashion.

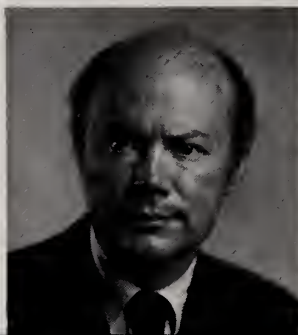
What a Compendium Should Contain

I believe the compendium should inform the doctor what a drug will do, when he should use for what type of patient, for how long, in what dose, what benefits his patient is likely to obtain, the risks involved, and cross-reaction with other drugs.

The information would be based on the package insert and have the same legal status. In fact a complete compendium with complete and current information might even eliminate the necessity

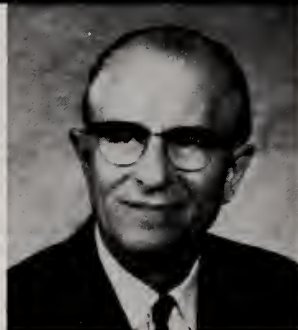
Government Health Official

Henry E. Simmons, M.D.
Deputy Assistant
Secretary for Health
Department of Health,
Education and Welfare



Maker of Medicine

Joseph F. Sadusk, Jr., M.D.
Warner-Lambert Company



A drug compendium, or preferably compendia, should, I believe, be private, not federal, in sponsorship. They should contain comprehensive listings of drugs available for prescribing. They should be single, legibly printed volumes of reasonable size, updated quarterly or semiannually and completely revised every year.

Function of a Compendium

A compendium should furnish the following information on drugs in the following order: indications for use, side effects, adverse drug reactions, contraindications, drug interactions, drug dosage at the dosage forms marketed. Drug prices should not be included because they vary so widely and change rapidly.

No compendium should set forth drugs of choice or discuss relative efficacy. Such questions must be left for the practicing physician to decide, whether on the basis of the medical literature, his own clinical experience, advice of colleagues, information supplied by manufacturers, and so on.

Nor should a compendium undertake to educate the doctor how to use drugs. Rather, it must be a reference source designed primarily to refresh his memory as to drugs he may not use regularly. It

or a package insert in many instances. This would constitute a substantial saving for the manufacturer.

By a complete compendium, do not mean a volume of prohibitive size. You don't need a book describing 25,000 products with an enormous amount of repetition. Rather, drugs should be arranged by class. Mutually applicable information would be provided, along with brief discussions pinpointing differences in specific drugs of that class. Listings would be cross-indexed in a useful way.

Other Available Documents as Sources of Information

Existing references such as DR and the AMA Drug Evaluation are obviously useful but they are incomplete. Either they are not cross-referenced by generic name and do not group drugs with similar characteristics, or they do not list all the available and legally marketed drugs. And some of those omitted may be very useful.

should in no way imply control over the practitioner's prerogatives.

Why Another Compendium?

A practicable, single-volume compendium cannot, nor is it necessary to, include all drugs on the market today. From my practice of internal medicine for some 25 years, my experience as a consultant, and as a faculty member of four or five medical schools, I would estimate that a doctor uses only 30 to 35 drugs regularly. The 1972 Physicians' Desk Reference, incidentally, contained about 2,500 entries.

As to whether there should be a federal compendium, in my opinion, as stated earlier, the answer is easy—there should *not* be one. The proposal assumes that existing compendia are inadequate. We're not sure of that at all. Whatever its imperfections, the present drug information system in the U.S. is open, multifaceted, pluralistic and extensive. Good compendia exist, as well as other ample sources on drug therapy, ranging from journal literature through AMA Drug Evaluation to company materials. Not all physicians may use such sources as often or as well as they should, but that is the fault of the man, not of the sources.

In any event, rather than pro-

On the other hand, drugs made by more than one supplier, tetracycline for example, may be fully described a dozen times in the same book.

While perhaps PDR could be rearranged and cross-indexed with generics included, and while the AMA Drug Evaluation might also be modified and expanded, I am not sure that the end result would have all the attributes required for a useful compendium. At the same time, you would run the risk of amassing a voluminous and unwieldy tome.

Should Editorial Comments Accompany the Listings?

Subjective judgments, in my opinion, have no place in a compendium. However, if there is substantial evidence based on a sound body of science concerning relative efficacy of several drugs, certainly that information should be included. The committee of experts compiling and editing a particular section would also have to assess

duce another book, it makes much more sense to work on improving existing compendia, and perhaps they could, as knowledge advances, include more accumulated clinical data and experience, and more information on drug interactions and adverse reactions.

Implications of a Federal Compendium

Take a hard look at the implications of a federal compendium. It would have the force of law, virtually dictating what drugs to use and how to use them. In effect, it would be a regulatory document with legal or quasi-legal status, posing medical/legal problems similar to those the doctor may now encounter if and when he departs from the provisions of the package insert. A compendium under federal aegis would tend to restrict decisions on drug therapy to one orthodox level—a most dangerous trend for medicine.

New Compendium — A Medical Option

I detect no ground swell of initiative or support whatsoever for a federal compendium—or, for that matter, for a new compendium of any type. A 1969 PMA survey conducted by Opinion Research Corporation found that only 15 per

and indicate instances where a meaningful difference between drugs is pertinent.

Sponsorship, Compilation and Editing

Producing a book like this would undoubtedly be difficult and demanding. It would obviously take a great deal of talent and expertise, and would require a varied and experienced group, ranging from writers and editors to highly skilled clinicians and pharmacologists. Style, format and clarity of language would play an important part in determining the usefulness of the book. And it should be updated periodically and completely revised annually.

I have no opinion whether the government or the private sector should sponsor and/or finance the compendium. What is most important is that the compendium be an authoritative, objective and useful source of information for the doctor to have at hand as a ready reference.

cent of those physicians interviewed felt a new compendium was needed. And a large majority did not favor the involvement of the federal government if one were to be created, preferring instead a nongovernmental consortium.

Even if we come to a time when the medical profession itself opts for a new kind of compendium, it should be handled and financed, ideally, outside both government and industry. Final review and editorial authority could be delegated, say, to specialty bodies and medical societies—but above all, *not* the government.

Surely the health care system in the United States has far more vital matters to consider than the extensive cost and effort that would have to go into the preparation and maintenance of a new, monolithic compendium, and especially one bearing the imprimatur of the federal government.

Opinion & Dialogue

What is your opinion, doctor? We would welcome your comments.

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PRESCRIBING INFORMATION

Antiminth (pyrantel pamoate) Oral Suspension

Actions. Antiminth (pyrantel pamoate) has demonstrated anthelmintic activity against *Enterobius vermicularis* (pinworm) and *Ascaris lumbricoides* (roundworm). The anthelmintic action is probably due to the neuromuscular blocking property of the drug.

Antiminth is partially absorbed after an oral dose. Plasma levels of unchanged drug are low. Peak levels (0.05-0.13 µg/ml.) are reached in 1-3 hours. Quantities greater than 50% of administered drug are excreted in feces as the unchanged form, whereas only 7% or less of the dose is found in urine as the unchanged form of the drug and its metabolites.

Indications. For the treatment of ascariasis (roundworm infection) and enterobiasis (pinworm infection).

Warnings. *Usage in Pregnancy:* Reproduction studies have been performed in animals and there was no evidence of propensity for harm to the fetus. The relevance to the human is not known.

There is no experience in pregnant women who have received this drug.

Precautions. Minor transient elevations of SGOT have occurred in a small percentage of patients. Therefore, this drug should be used with caution in patients with pre-existing liver dysfunction.

Adverse Reactions. The most frequently encountered adverse reactions are related to the gastrointestinal system.

Gastrointestinal and hepatic reactions: anorexia, nausea, vomiting, gastralgia, abdominal cramps, diarrhea and tenesmus, transient elevation of SGOT.

CNS reactions: headache, dizziness, drowsiness, and insomnia. Skin reactions: rashes.

Dosage and Administration. *Children and Adults:* Antiminth Oral Suspension (50 mg. of pyrantel base/ml.) should be administered in a single dose of 11 mg. of pyrantel base per kg. of body weight (or 5 mg./lb.); maximum total dose 1 gram. This corresponds to a simplified dosage regimen of 1 cc. of Antiminth per 10 lb. of body weight. (One teaspoonful = 5 cc.)

Antiminth (pyrantel pamoate) Oral Suspension may be administered without regard to ingestion of food or time of day; and purging is not necessary prior to, during, or after therapy. It may be taken with milk or fruit juices. Because of limited data on repeated doses, no recommendations can be made.

How Supplied. Antiminth is available as a pleasant tasting caramel-flavored suspension which contains the equivalent of 50 mg. pyrantel base per ml., supplied in 60 cc. bottles.

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WORMS BLITZED



A single dose of Antiminth (1 cc. per 10 lbs. of body weight, 1 tsp./50 lbs. — maximum dose, 4 tsp.=20 cc.) offers highly effective control of *both* pinworms and roundworms.

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One prescription can economically treat the entire family.

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*Warning—may be habit-forming. Each tablet also contains: aspirin gr. 3½, phenacetin gr. 2½, caffeine gr. ½.

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#3, codeine phosphate* (32.4 mg.) gr. ½
#4, codeine phosphate* (64.8 mg.) gr. 1

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Who did successfully testify against a headlong rush into a large-scale HMO program?

Who did propose a program of *voluntary* national health insurance and succeeded in enlisting more Congressional co-sponsors for it than any

other national health insurance bill?

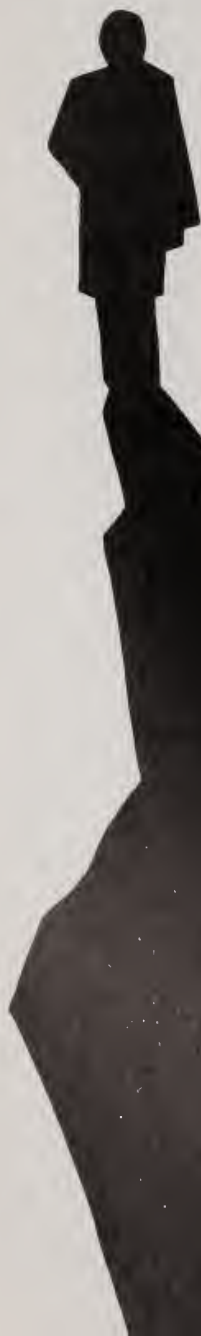
Who did propose the development of nationwide community emergency medical services? Who did promote maternal and child care programs? Federal aid to medical schools? Stronger occupational health and safety laws?

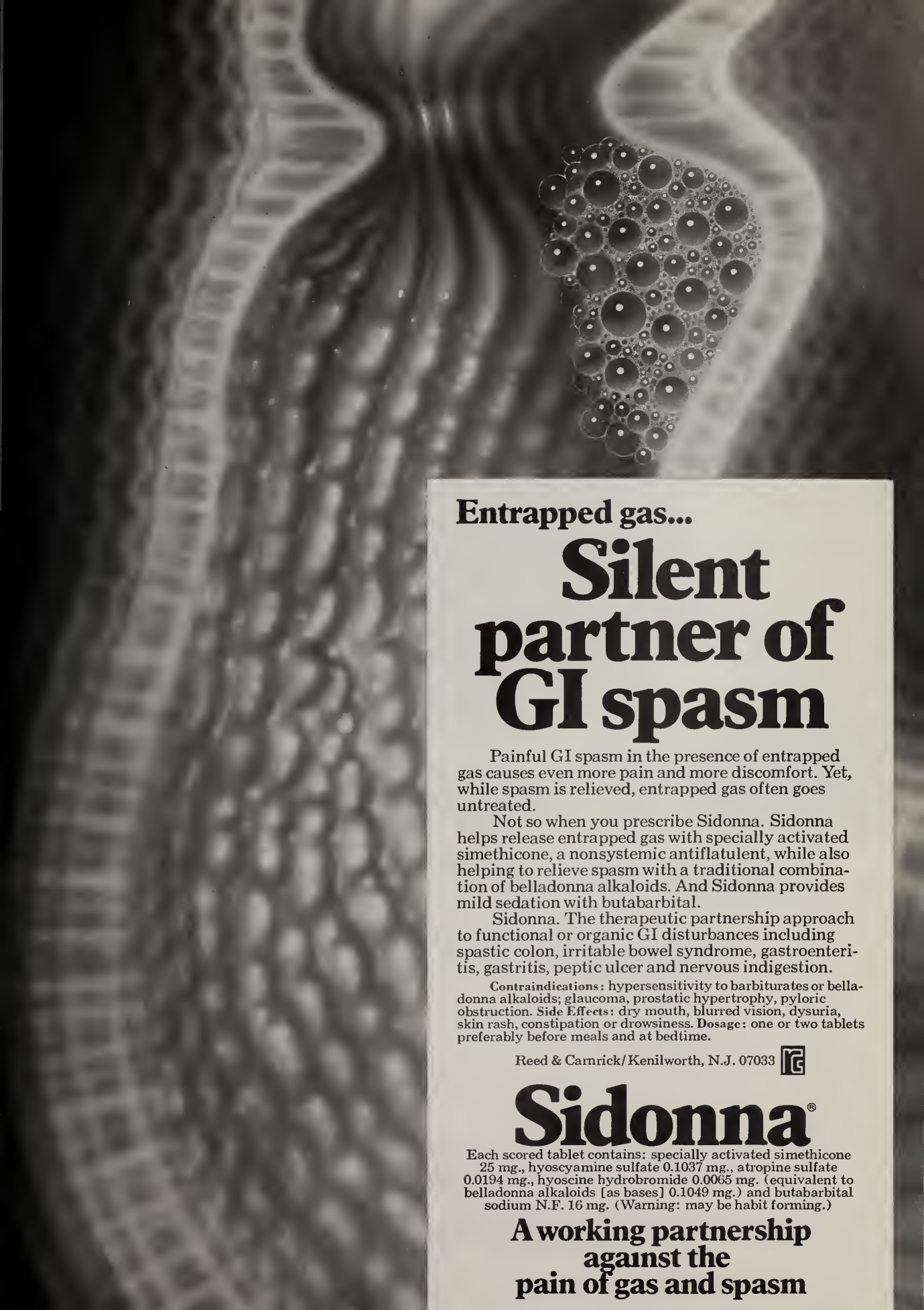
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THE VIEW BOX

(from page 294)

DIAGNOSIS: Neurinoma (Neurilemoma, Schwannoma)

Note in the chest film the sharply outlined posterior gutter mass at the D3 level on the right. This led to examination of the spine which showed an enlarged neural foramen and minimal pressure deformity of the adjacent rib. A Myelogram revealed an intradural-extramedullary defect.

The vast majority of posterior mediastinal masses are neurogenic in origin and the most common neurogenic tumors are neurinomas (more often in the young) and meningiomas (more often in the older age group). Gliomas occur much less frequently than in the brain.

Neurinomas probably arise from cells of the nerve sheath and can compress the spinal cord and often extend outside the bone spinal canal (Dumbbell tumor). They are benign, sharp in outline and usually do not calcify.

*Edited by Gunther J. Augustin, M.D.
Senior Attending Radiologist, Washington
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ECG PROBLEMS

(from page 306)

INTERPRETATION: 1. Old septal myocardial scarring.
2. Left axis shift, probably representing left anterior hemiblock.

The absence of initial R wave in leads V_1-V_3 with only a tiny R wave in V_4 indicates abnormality of the initial depolarizing forces within the septum and adjacent portions of the anterior wall of the left ventricle. This indicates myocardial scarring, usually produced by myocardial infarction. In addition, the frontal axis is approximately -50° . This is significantly deviated to the left. One of the prominent causes of significant left axis shift is left anterior hemiblock. This is consistent with septal myocardial infarction, and suggests that the anterior fascicle of the left bundle branch was destroyed at the time of septal myocardial infarction. There are no ST or T changes in this electrocardiogram which suggest that the infarction may be recent (another "routine" electrocardiogram dated 6/12/73 was discovered. It is essentially identical with this one, further indicating that the septal process is old).

Edited by
Robert R. Montgomery, M.D.

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INDEX TO ADVERTISERS

Insurance

Corroon & Black, Russell, Inc	8
Ralph W. Lee & Company	T-335
Mutual of Omaha	4

Nurse Registries

District of Columbia Manpower Administration	T-338
---	-------

Nutrition Education

Dairy Council of Greater Metropolitan Washington, D.C.	2
---	---

Pharmaceuticals

Abbott Laboratories	T-321
Burroughs Wellcome & Company	T-328
Burton, Parsons & Company, Inc	T-334
Dorsey Laboratories	T-329

Eli Lilly & Company	12
McNeil Laboratories	9
Pharmaceutical Manufacturers Association	T-324
Reed & Carnrick	T-331
Roche Laboratories	C2, 1, T322
J. B. Roerig	C3, C4
The Upjohn Company	T-326-T-327

Pharmacy

Peoples Drug Stores	T-336
---------------------	-------

Sanitarium

Kalorama Convalescent Home Inc	T-338
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Therapy

The University Center	T-333
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Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

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CONTENTS

SCIENTIFIC ARTICLES

Thermal Burns in Children. Judson G. Randolph, M.D., William P. Tunell, M.D. and John R. Lilly, M.D.	341
Experiences with Transportation of the High-Risk Newborn. Glenn Blackburn, M.D., Maureen C. Edwards, M.D., Anne B. Fletcher, M.D. and Gordon Avery, M.D.	349
A Survey of Immunization Status of Children Enrolled in a Comprehensive Health Clinic. J. Wm. Oberman, M.D.	353
Use of the High Plus Bausch and Lomb Softlens[®] in the Management of Aphakia in Infants and Children. David S. Friendly, M.D., Blackwell S. Bruner, M.D., Thomas Frey, M.D., Martin E. Lederman, M.D., Marshall M. Parks, M.D., and Nevin Oldt	359

SPECIAL ARTICLE

Acupuncture for Deafness: A Study of Patients Treated in Washington, D. C. David Fairbanks, M.D., Ellis A. Wallenberg, M.S. and Blair M. Webb, M.D.	367
---	-----

OTHER FEATURES

Editorial J. William Oberman, M.D.	5
Scientific Editorial James A. Curtin, M.D.	7
The View Box Edited by Gunther J. Augustin, M.D.	348
ECG Problems Edited by Robert F. Montgomery, M.D.	352
Book Reviews Gastrointestinal Pathology. (Morson and Dawson) Reviewed by Thomas S. Sappington, M.D. Manual of Cardiac Arrhythmias. (Bilitch) Reviewed by Jorge C. Rios-Pradier, M.D. The Use of X-ray Techniques in Forensic Investigations. (Graham) Reviewed by George Tievsky, M.S.	381
Information for Authors	384
Advertising and Subscription Information	384
Index to Advertisers	388

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Editorial

The ultimate purpose and first priority of any medical institution must be the care and amelioration of illness in patients entrusted to its care. Of late, however, there has been increasing pressure generated both from within the medical establishment and the community it serves to expand this role. Hospitals now are being urged to think in the broader terms of prevention of disease and the maintenance of health. In many instances this has resulted directly in the development of hospital-sponsored programs for the delivery of comprehensive health care. The administrative vehicle frequently is a health maintenance organization.

As we have gained experience in operating these programs we have become aware of at least two major problems: 1) glaring deficiencies in the actual delivery of individual health services, particularly for low income groups, and 2) the difficulty many communities have in planning for the health needs of their citizens. A complete answer to these problems lies in the future, and probably awaits the development of some form of national health insurance. In the meantime, however, hospital staffs are joining other members of the medical profession, public health authorities and the community-at-large in both advocating and working toward ensuring that quality health care be made available to all.

A large teaching hospital or medical center has an additional challenge. Traditionally a leader in

developing research and training programs to meet the needs of the *individual* for medical care, it now must use a portion of its resources to plan, carry out and evaluate the effectiveness of programs designed to meet the health needs of *groups of individuals*. These groups may live in a neighborhood (primary care), be referred from private practitioners as well as from an entire geographic region (highly specialized tertiary care). Concomitantly, it must be prepared to train the many new kinds of physicians and allied health workers necessary to staff these innovative programs.

We at the Children's Hospital National Medical Center believe that the articles contributed to this issue of the Annals exemplify the range of endeavors with which a modern medical center must concern itself. The Department of Ophthalmology is represented by a paper from Friendly et al which describes the contribution a pediatric teaching institution can make toward evaluating the effectiveness of newer methods of treatment. The three remaining articles detail how a children's medical center can improve the health and well-being of a community of children, by functioning both as a provider of primary care to children living in a local inner-city area (Oberman) and as a regional referral center giving highly specialized team care to two particularly vulnerable groups of children (Blackburn et al, Randolph, Tunnell & Lilly).

J. William Oberman, M.D.

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SCIENTIFIC Editorial

CLINDAMYCIN

Clindamycin, a 7-chloro derivative of Lincomycin, has steadily replaced its predecessor in the field of antibiotic medicine. For example, at one hospital eight times as much Clindamycin was used in 1973 compared to Lincomycin, based upon total therapeutic units.

This group of drugs has as its major primary indication the treatment of anaerobic infections, particularly those due to *Bacteroides fragilis* and other sensitive *Bacteroides* species. Our experience, similar to that of other observers, is that this is an effective agent in the management of serious infections due to, such as septicemia or lipo-pulmonary infections. It is suggested that Clindamycin is more effective than Lincomycin and Chloramphenicol in the clinical setting of anaerobic infections because it is not inhibited by low tissue oxygen and lactic acid as are other drugs. The sites and types of infections frequently associated with anaerobic organisms, particularly *Bacteroides*, have been well described in the literature over the past several years. These observations, while not new ones, have been better documented by improved anaerobic microbiological techniques.

The various clues for anaerobic infections include pus with a fecal odor, gas in tissues, infections following pelvic surgery or instrumentation, infections after large bowel surgery or trauma, and infection that occurs or persists while a patient is receiving adequate coverage with antibiotics for aerobic flora, e.g. Gentamicin. The laboratory can be of assistance in suggesting this diagnosis from a gram stain of purulent material since the morphology of the gram negative rods may raise the possibility of a *Bacteroides* infection.

Both Lincomycin and Clindamycin have been implied as a cause of diarrhea in a significant percentage of patients. In most instances this is self limited and clears quickly when the agent is stopped. However, in some instances there has developed a picture very similar to acute ulcerative colitis on sigmoidoscopy and biopsy examination. There have also been cases of pseudomembranous enterocolitis associated with these drugs. This usually follows oral

use of the drug, but a similar picture can develop in patients who have received the agent parenterally.

Other indications for use include staphylococcal osteomyelitis; these drugs have been used successfully, at times, for serious staphylococcal infections which have failed to respond to first line antistaphylococcal drugs. Most authorities still prefer to use Penicillin, or a penicillinase resistant Penicillin or Cephalothin, for serious Staphylococcal infections, but under certain conditions (particularly drug hypersensitivity or treatment failure) the use of Clindamycin may be warranted, particularly if renal disease precludes the use of Vancomycin.

There have been reports of Mycoplasma pneumonia responding to Clindamycin. It is also effective against the *Pneumococcus* and *Streptococcus*, and can be used as a substitute in such infections in patients allergic to Penicillin. However, in view of the problem with diarrhea, and until the incidence of an ulcerative colitis-like reaction is more clearly defined, it would seem reasonable to use an agent such as Erythromycin for less serious infections in the allergic patient.

Lincomycin has been used in the management of bacterial meningitis due to *Pneumococcus*. The data for Clindamycin indicate that this agent should not be used for meningitis because of poor diffusion across the blood-cerebro-spinal fluid barrier. Therefore, Chloramphenicol remains the drug of choice for *Bacteroides* infection of the central nervous system.

In summary, Clindamycin has replaced Lincomycin in our therapeutic armamentarium. It can be given both orally and parenterally. It is usually well tolerated with the most significant side effects involving the gastrointestinal tract. It is a very effective and usually safe agent, particularly in the management of *Bacteroides* infections and in certain types of staphylococcal infections. Resistance may emerge to this agent and although it has not been a major problem at the moment judicious use of the drug is warranted. Since it competes with Erythromycin for the same binding site in the microbe these two agents should not be used simultaneously.

Methicillin resistant strains of *Staphylococci* are usually sensitive to Clindamycin. In patients with renal failure the half life of the drug is prolonged and therefore the dose should be reduced. However, there seems to be considerable tolerance of this particular agent, even at high blood levels.

If the use of this drug is limited to appropriate

indications unpleasant and dangerous side effects will be avoided and its antimicrobial efficacy will be preserved.

James A. Curtin, M.D.

*Chairman, Department of Medicine
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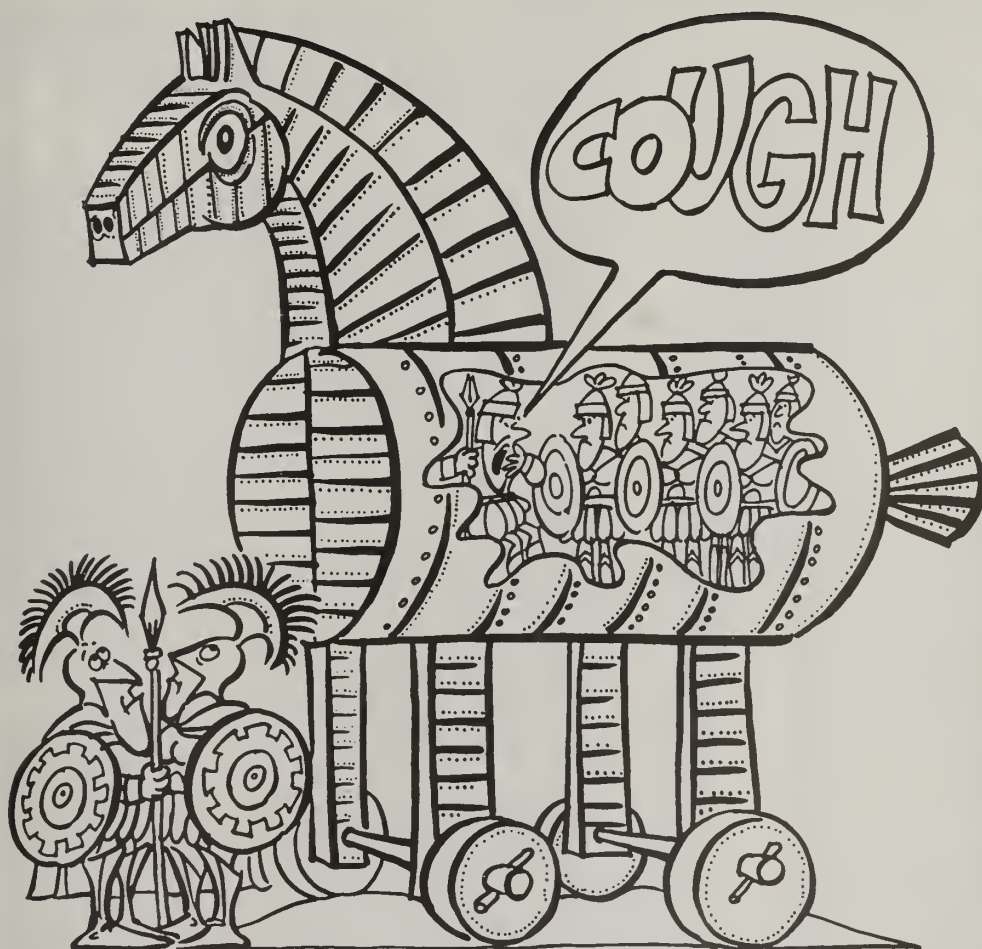
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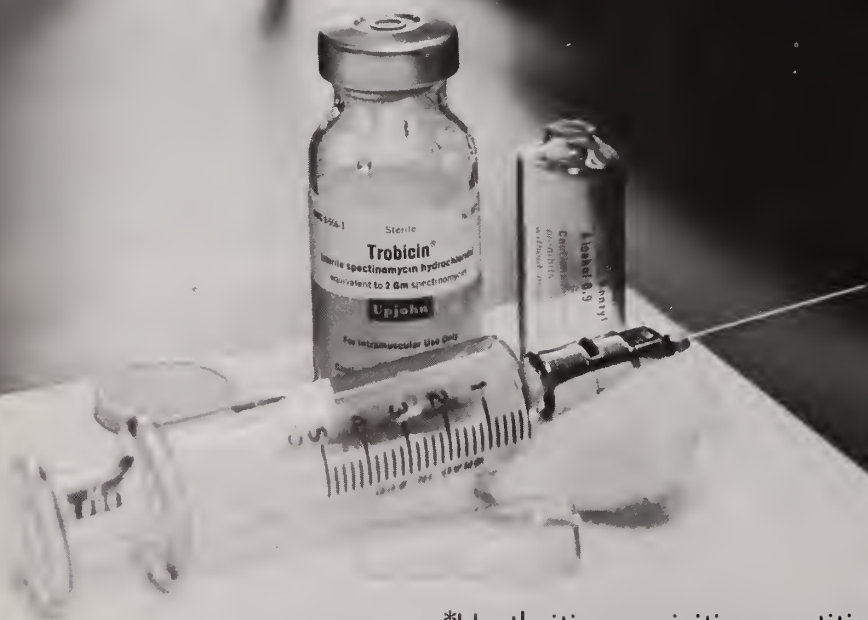
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Warnings: Not indicated for the treatment of syphilis. Antibiotics used to treat gonorrhea may mask or delay the symptoms of incubating syphilis. Patients should be carefully examined and monthly serological follow-up for at least 3 months should be instituted if the diagnosis of

syphilis is suspected.

Safety for use in infants, children and pregnant women has not been established.

Precautions: The usual precautions should be observed with atopic individuals. Clinical effectiveness should be monitored to detect evidence of development of resistance by *N. gonorrhoeae*.

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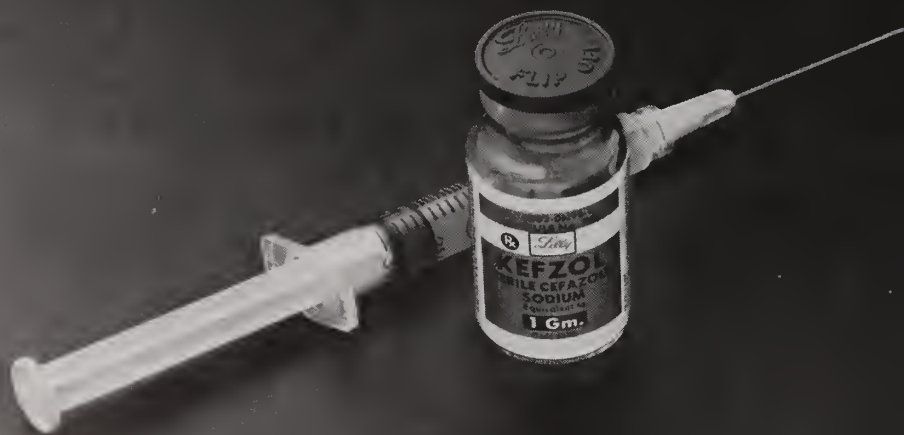
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[†]For patients with gonorrheal proctitis and for patients in geographic areas where antibiotic resistance is known to be prevalent, initial treatment with 4 grams is preferred.

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SCIENTIFIC ARTICLES

Thermal Burns in Children

JUDSON G. RANDOLPH, M.D., WILLIAM P. TUNELL, M.D. AND JOHN R. LILLY, M.D.

Abstract

Trauma is the leading cause of death in childhood years with burns second only to transportation accidents in accidental death. Over 2000 children die from burns each year in the United States. Experience at the Burn Unit established at the Children's Hospital National Medical Center shows two major groups, the first in the 18 months to three year age group with scalds. The second group, although not so large, contains the most severely injured. These are the five or six year olds who have sustained a flame burn, often because of their curiosity about matches. Because children's clothing is usually not flame-retardant, most fabrics will burn in a matter of seconds, almost always causing full-thickness skin damage.

The children have been treated in the Burn Unit with topical antibiotics, supportive intravenous care, subsequent debridement under general anesthesia, and finally grafting. The supporting services of Sociology, Psychiatry and Physical Medicine contribute enormously to the total care of the burned child. The goal is to return to his home a child who is able to move all joints, has minimal scarring and disfigurement, and who has had a vigorous program of psychological and physical rehabilitation.

In 1965, a Burn Unit was established to foster optimal care of children with major thermal injury. The purposes... are to describe a five year experience of this unit and to outline methods of burn management in children which have proven beneficial in this burn facility.

Introduction

8,000 Americans (2,000 of them children) die each year of burns.¹ Burns, in fact, are second only to transportation accidents as the leading cause of traumatic death in children.

In 1965, a Burn Unit was established at the Children's Hospital National Medical Center to foster optimal care of children admitted to the Hospital with major thermal injury. The purposes of this paper are to describe a five year experience of this unit and to outline current methods of burn management in children which have proven beneficial in this burn facility.

Clinical Observations

The patient group demonstrates that there are two major groups of children suffering thermal burns. The

first and largest group is that containing children from eighteen months to three years who suffer scalds. These curious children crawl and toddle in the kitchen or, at mealtimes, pull up on parents who may be drinking hot liquids like coffee or tea. Thus, they are at high risk from boiling water pulled from the stove or hot coffee or tea in the pot or in the cup. It is of interest that boiling liquid, removed from the stove and having been poured once from container to cup usually is cool enough to cause only a second degree burn. In contrast, the pots which are pulled from the stove may cause a full thickness injury.

The second group of children, although not as numerous, comprise the most severe injuries. These children are five or six years of age and have the same curiosity as the younger child, but direct that curiosity toward matches. They play with matches secretly, away from the parent, and all too often light their clothing. Because children's clothing is usually not flame retardant, most of the fabrics will burn from the child in a matter of seconds. This almost always causes full thickness skin damage.

In addition to these two main causes of burn injury in the group of children in the present study, there are the other typical causes of thermal injuries of childhood such as explosions, house fires, high voltage electri-

THERMAL BURNS IN CHILDREN

RANDOLPH, TUNELL AND LILLY

cal injuries and caustic liquids in contact with the skin.

Patient Data

184 children with thermal burns were admitted to the Burn Unit at Children's Hospital of the District of Columbia from 1966 through 1970 (Tables I and II). Sixty-one percent were male, 54% were under three years of age. Flame burns accounted for 44 patients, or 24% of the total burns, but eight of the ten deaths in the series. On the contrary, scalds were the cause of injuries in 87 patients, 48% of the total, but of only two of the ten deaths. Sixty percent of the burns which occurred in children under three years of age were caused by scalding.

Table III relates age, sex, etiology of the burn and cause of death. Although 54% of the patients admitted were under three years of age, only one death came from that age group. That patient sustained the most common injury for his age group (a scald burn) and died of a Curling's ulcer after eight days of hospitalization. As has been noted, eight of the ten deaths occurred in the patients with flame burns. All of the deaths in patients over four years of age were in children with flame injuries.

Each of the patients in this series who expired did so during the original hospitalization. Two children died in the first 48 hours following admission; one with a pulmonary burn, the second with 95% body surface burns. Each of the four patients who survived longer than one month ultimately died of sepsis and its complications. (Table IV)

Patient Management

The management of burn patients may be categorized into post-burn time periods. The principal derange-

ments, symptoms and their solution vary in general with these time periods. Although overlap occurs, the following divisions have been found useful in focusing on the salient features of burn care. (Table V).

I. Shock Phase

The initial 48 hours following a severe burn is characterized by the

Table I: Children's Hospital Burns 1966 - 1970

Etiology	Number	Mortality
Water Scald	87	2 (2.3%)
Flame	44	8 (18%)
Other	53	0
Total	184	10 (5.4%)

TABLE II: Children's Hospital Burns 1966 - 1970

Surface Area and Mortality			
% Surface Burn	Number	# Deaths	Mortality Rate %
under 6	69	0	0
6-15	62	1	1.6
16-45	41	3	7
46-80	10	4	40
over 80	2	2	100
	184	10	5.4

TABLE III: Children's Hospital Burns 1966 - 1970

Deaths				
Age	Sex	Burn Etiology	Cause of Death	% Burn
2	M	Scald	Curling's ulcer	45
4	M	Scald	Shock (adm 1 day post burn)	40
4	M	Flame	Shock	95
6	M	Flame	Sepsis	45
6	F	Flame	Sepsis- <i>Pseudomonas</i>	60
6	F	Flame	Sepsis	80
7	M	Flame	Pulmonary burn	15
7	F	Flame	Aspiration	50
9	F	Flame	Sepsis-s. <i>Aureus</i>	30
13	M	Flame	Sepsis- <i>Pseudomonas</i>	65

frequent shock and death which occur if adequate therapy is not given. Satisfactory fluid resuscitation has evolved despite the lack of an entirely clear notion of precise fluid, protein and electrolyte changes in the burn patient's wound. A number of formulas have been devised as guides to intravenous replacement of burn wounds^{2,3,4,5}. If resuscitation is to be performed satisfactorily, the formulas must be considered strictly as guides and not as rules of therapy. Each of the formulas attempts an isotonic salt replacement of plasma lost into the burn wound. Each also provides additional electrolytes with free water to meet baseline requirements and to replace those losses attendant on the hyperdynamic postburn state. Adequacy of therapy is determined by a number of useful clinical guidelines including urinary output and central venous pressure. Many of the mechanisms of renal function and water balance are as yet not fully understood. Urinary output is therefore a valuable but not necessarily the most valuable possible measure of resuscitation. Other parameters such as arteriovenous oxygen difference and base deficit have allowed more precise methods of resuscitation, and have been particularly useful in patients

TABLE IV: Children's Hospital Burns 1966 - 1970

Mortality by Time Post Burn		
Post Burn Day Death	% Burn	Cause of Death
2	15	Pulmonary burn
2	95	Shock
7	30	Sepsis
7	40	Shock
8	45	Curling's ulcer
28	50	Aspiration
32	45	Sepsis
37	65	Sepsis
60	60	Sepsis
212	80	Sepsis

with pulmonary burns and in patients with "shock lung" secondary to surface injury.

As is customary in most burn units, on arrival the patients are undressed and grossly cleaned of bits of clothing and dead skin. An accurate weight is obtained and an indwelling urinary bladder catheter is placed. The latter is essential in children for the accurate determination of hourly urinary output. Intravenous fluid routes are begun and in the more severely burned

patients are positioned into the central venous pool. Tetanus prophylaxis is given and a five day course of penicillin is begun.

Fluid resuscitation is begun with the Evan's formula modified for the increased burn wound losses seen in small children. (Table VI) Volume is adjusted to obtain an adequate urinary output, considered to be 10 or 15 milliliters per hour in the small child and 20 to 30 milliliters per hour in the larger child. Resuscitation incorporating adequate hydration and, if necessary, diuresis, promotes a consistently adequate urinary output and is crucial in protecting against the onset of renal failure in the postburn period.

A pulmonary burn greatly increases chances of death in this shock period but was seen only once in our series. The scald or the sudden, shortlived flame burn of clothing involving trunk, arms and neck seldom produce a significantly pulmonary burn. Only rarely will burns about the mouth and nose interfere with respiration. In addition, the enveloping deep fascia of the neck usually protects the airway from the substantial edema of the neck which follows a burn of that part. Thus, the incidence of necessary tracheostomy is quite low. Tracheost-

Table VI: Children's Hospital Burns 1966-1970

Fluid Replacement	
I	First 24 hours
A.	Dynamic loss
	1. Colloid (as plasma or plasma substitute)
	1.0 ml/kg. weight/% burn
	plus
	2. Electrolyte (as Lactated Ringers solution)
	1.0 ml/kg weight/% burn
B.	"Baseline" (as 5% D/W)
	To 15 kg body weight—120 ml/kg
	Over 15 kg body weight—80 ml/kg
II.	Second 24 hours
	Decrease "Dynamic Loss" by ½

Notes

1. Calculate to maximum 50% body surface burn
2. Children under 15 kg can be expected to have "Dynamic Losses" exceeding those calculated above.

omy is not done unless absolutely essential as it has been shown to promote infection of the pulmonary tree, particularly if it is necessary to place a tracheostomy tube through an area of the burn wound.

II. Period of Infection

The interval of three to four weeks following the shock phase is conventionally labeled the period of infection. During this time the burn wound becomes infected and may seed to the circulation and other organ systems. Beginning with Dr. Carl Moyer's 1965 report of one half percent silver nitrate solution as a topical antibacterial agent, a number of such materials have been used in the treatment of burn wound infection^{6,7,8,9}. These have

TABLE V: Children's Hospital Burns 1966 - 1970

The Time Sequence Following a Major Burn				
	1	2	3	4
	48 hr.	3-28 days	15-45 days	Months-Years
Symptom	Shock	Infection	Malnutrition (& infection)	Physical Scar Psychological
Treatment	Fluids	1. Debridement surgical chemical 2. Dressings 3. Excision	Skin Coverage homograft autograft	1. Physiotherapy 2. Reconstructive Surgery 3. Psychotherapy

THERMAL BURNS IN CHILDREN

RANDOLPH, TUNELL AND LILLY



Fig. 1. Fifteen month old who pulled a coffee pot over sustaining second degree burns of the face.

generally been helpful in suppressing the devastating systemic infections seen so frequently prior to their introduction. Some features are common to all such agents thus far developed. They do not sterilize the third degree scar but do reduce bacterial infection to a varying degree. Biopsy of the burn wound-non burn interface later than 48 hours post burn invariably shows bacterial coloniza-

tion. The emergence of the resistant bacterial strains, especially *Pseudomonas*, has occurred with most of the currently used agents. Moreover, topical antibiotics has lengthened the period of eschar separation. Most burn surgeons feel complete excision of the wound eschar by the end of the fourth week is desirable. With the use of topical antibacterial agents, it may be necessary to aggressively surgically

debride the wound to achieve complete excision by this time. Topical antibacterial agents have improved survival in the moderately extensive burn but have not permitted substantial increase in survival rates for the massive burn of 70% or more of the body surface.

From 1966 to mid-1969, burns at Children's Hospital were treated with topical one half percent silver nitrate solution. Since that date, Sulfamylon cream has been used. With each of these agents, it was necessary to supplement ward debridement, done daily at the time of whirlpool bath, with at least one debridement under general anesthesia. In extensively burned patients, debridement was begun 10 to 14 days post-burn and completed in approximately two weeks. Autografting, if possible, was done concomitantly. On several occasions, parental skin was taken and used as homograft dressing until autograft coverage was complete. Currently, Betadine cream and silver Sulfadiazine cream are under clinical study.

Urine verdoglobulin determinations were useful in predicting *Pseudomonas* sepsis. With the receipt of a positive urine verdoglobulin report, systemic antibiotic treatment was begun. It was commonly Carbenicillin but in extreme cases included Gentamicin or Polymyxin B.

III. Malnutrition and Infection

Even as infection remains a continuing problem in the severely burned patient, protein loss from the unhealed wound and caloric expenditures from surface evaporation persist. Malnutrition becomes evident with weight loss, hypoproteinemia and anemia and continues until healing has closed all but approximately 10% of the body surface area. High protein feedings, vitamins C and A and occasional trans-



Fig. 2. Three year old, allowed to draw her own bathwater, sustaining second and third degree burns from overheated water.



Fig. 3. Five year old with burns suffered when non-flame retardant pajamas caught fire. This child was playing with matches and sustained the characteristic trunk, axilla, neck and face burn seen when clothing ignites.

fusions of albumin and whole blood are necessary. Young patients will frequently eat well with parental encouragement. The regular hospital diet has been supplemented with vitamins and liquid high protein supplements. On occasion, nasogastric caloric augmentation has been necessary. Intravenous hyperalimentation gained popularity during this period but was not used in this series of burn patients. Caloric expenditure was also lessened by the use of a warm humid environment. Recent work suggests that an environment which diminishes evaporative heat loss may spare calories¹⁰. The keystone in the reversing of malnutrition remains wound healing and skin coverage.

Throughout these three phases, it is the nursing department which bears the brunt of the effort. Only with dedicated, highly-skilled nurses can the children with major burns be brought safely through their ordeal.

IV. Period of Rehabilitation

Rehabilitation of the burn patient, both physically and psychologically, optimally begins on the day of the burn.

At Children's Hospital, the Physical Therapy and Occupational Therapy Departments maintain an active program of appropriate mobilization and immobilization. Exercise of the part is begun 48 to 72 hours after burn injury, is continued daily, and is reinstituted as soon as possible after grafting procedures. Motion and exercises were encouraged at the time of the daily whirlpool bath in nearly all of the patients in the series.

Patient follow up is provided by a twice monthly Burn Clinic run jointly by the Departments of General Surgery, Plastic Surgery, and Orthopedic Surgery. At these clinics determina-

THERMAL BURNS IN CHILDREN

RANDOLPH, TUNELL AND LILLY

tions for further reconstructive or cosmetic surgery are made and the patient's admission arranged.

Little is known about the psychological scarring of the child severely ill with a recent burn who is separated from his family and his needed emotional support when thrust into a busy hospital burn unit. We consider parental visits indispensable in helping the children adjust to their indefinite stay in the Burn Unit. Play therapists advised by the psychiatric service are active with our burned children. In general, children adjust fairly well to the Burn Unit. Many of our discharged patients return to visit the nursing staff.

Life must also be difficult for the disfigured and scarred burn patient. Other children can be cruel and parents may find it difficult to conceal their revulsion. Upon discharge, the

Visiting Nurse Service begins home visits to counsel the family in care of the patient and in developing healthy attitudes towards these children. These are small but important steps in the adjustments of the child and his family.

Discussion

We have been particularly cognizant in recent years of significant progress in the ability to handle the immediate effects of burns and to rescue patients from what has previously been fatal injury. However, as children with the massive burns are followed, the limitations of the care team in minimizing both the physical and psychological effects of the heat injury become apparent. Plastic surgical procedures can be utilized to remove or modify serious contractures of the growing

limbs and can eliminate many of the more serious scars and blemishes. However, the child endures weeks, months, and years of surgical therapy. In spite of the best efforts, these young patients are disfigured for life and carry this knowledge and its attendant psychological trauma during the final development of the adult personality. Herein lies the real tragedy of the burned child. In spite of many advances in burn care, the final result, particularly for a child, is often unsatisfactory. The search must continue for ways to prevent these injuries since our best efforts, couched as they are in extended, expensive hospitalization, leave much to be desired in the final outcome.

Summary

The burn experience at the Children's Hospital of the District of Columbia for the years 1966 to 1970 has been presented. The mode of therapy for 184 patients has been reviewed and the current Children's Hospital care policy has been described.



Fig. 4. One year old child whose burn is being treated by the open technique using Sulfamylon. Note the use of nasogastric tube, an essential in the early days of management of burned babies and young children.

References

1. ARTZ, C. P., MONCRIEF, J. A.: The treatment of burns. Philadelphia, Pa., W. B. Saunders Co., 1969.
2. EVANS, E. I., PURNELL, O. J., ROBINETT, P. W., BATCHELOR, A., MARTIN, M.: Fluid and electrolyte requirements in severe burns. *Ann. Surg.* 1952, 135:804.
3. REISS, E., STIRMAN, J. A., ARTZ, C. P., DAVIS, J. H., AMSPACHER, W. H.: Fluid and electrolyte balance in burns. *J.A.M.A.*, 1953, 152:1309.
4. BAXTER, C. R., SHIRES, T.: Physiological response to crystalloid resuscitation of severe burns. *Ann. N. Y. Acad. Sc.* 1968, 140:874.



Fig. 5A. Mixed burn of legs and trunk.

5. MOORE, F. D.: The body-weight burn budget. *Surg. Clinics No. Am.* 1970, 50:1249.
6. MOYER, C. A., BRETANO, L., GRAVENS, D. L., MARGRAFF, H. W., MONAFO, W. W., JR.: Treatment of large human burns with 0.5% silver nitrate solution. *Arch. Surg.* 1965, 90:812.
7. STONE, H. H., MARTIN, J. D., JR., HUGER, W. E., KOLB, L.: Gentamicin sulfate in the treatment of pseudomonas sepsis in burns. *Surg. Gynec. Obstet.* 1965, 120:351.
8. MONCRIEF, J. A., LINDBERG, R. B., SWITZER, W. E., PRUITT, B. A.: The use of topical antibacterial therapy in the treatment of the burn wound. *Arch. Surg.* 1966, 92:558.
9. FOX, C. L.: Silver sulfadiazine — A new topical therapy for pseudomonas in burns. *Arch. Surg.* 1968, 96:184.
10. BARR, P. O., BIRKE, G., LILJEDAHL, S. O., PLANTIN, L. O.: Oxygen consumption and water loss during treatment of burns with warm dry air. *Lancet* 1968, 1:164.



Fig. 5B. Same child 34 days after open treatment. Some epithelialization has occurred at edges of third degree injury. Second degree burn has healed and patient is ready for autografting.

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THE VIEW BOX

Prepared by The Department of Radiology Washington Hospital Center

A fifty-one year old alcoholic man who presented with retrosternal chest pain developing after several bouts of emesis. Physical examination revealed left lower lung field dulness with crepitus palpable over the nuchal and supraclavicular regions.

(for diagnosis see page 358)

Film #1



Film #2



Experiences with Transportation of the High-Risk Newborn

GLENN BLACKBURN, M.D., MAUREEN C. EDWARDS, M.D., ANNE B. FLETCHER, M.D. AND GORDON B. AVERY, M.D.

Abstract

Nearly one-third of all infant deaths occur within the first 24 hours of life. Early and proper treatment of many conditions does, however, alter outcome favorably. For this reason, early transportation of sick newborns is recommended.

In February 1972, Children's Hospital National Medical Center established an Infant Transport System utilizing a specially equipped van accompanied by personnel trained in the care of the critically ill newborn. This service has been utilized by transferring hospitals throughout the greater Washington area. In the first two years of operation, 294 newborns have travelled in the van. It is felt that infants arrive at Children's Hospital National Medical Center nursery earlier, warmer, and in better general condition than by conventional transfer means.

Introduction

Rapid advances in the care of the neonate in the last decade have accentuated the need for regional newborn intensive care centers where highly specialized equipment and personnel are readily available. In the last five years, there have been major refinements in the transport incubator, permitting the infant to be kept warm

and well-oxygenated even while rendering necessary care during transit. Finally, the development of a mobile van equipped with intensive care facilities has permitted safer transportation of sick infants to the regional intensive care nursery.

Admittedly, this is not the ideal situation for the mother or the infant. Infants delivered in hospitals with intramural newborn intensive care units have the lowest morbidity and mortality rates. However, the ex-

The subjective opinion. . . is that the infants transferred by van to the hospital arrive earlier, warmer, and in better general condition than pre-van experiences.

tremely high cost of specialized physicians and nurses, as well as equipment, makes this type of organization impossible in every hospital that delivers babies. The uterus is the ideal "transport incubator," and ideally high-risk mothers should be delivered at centers with both maternal and infant intensive care units. This would eliminate 40% of the problem deliveries in small hospitals. Yet some infants develop difficulty following seemingly normal gestation, labor, and delivery.

For these reasons, the Children's Hospital National Medical Center established an Infant Transport System, made possible by a gift from the Marathon Bridge Club. Prior to the initiation of the Infant Transport System, seriously ill neonates were transferred to this institution via local ambulance services, frequently accompanied by unskilled personnel, and often hypothermic, hypoxic, and apneic. Experiences with this transport service, in operation since February 1972, are reported below.

Infant Transport Van

The van, a modified Chevrolet delivery van fitted with a fiberglass top to give standard head room, is equipped with a battery or AC powered Ohio Transport Incubator capable of achieving ambient temperatures in excess of 90° Fahrenheit. Portable oxygen tanks, attached to the incubator or the large standing tank in the van, achieve oxygen levels up to 90% in the incubator. A gasoline powered auxiliary generator providing 110 Volt AC electricity powers the incubator during transit and supports extra lighting and the Gomco electric suction pump. Other equipment in the van includes a cardiac monitor, an oxygen analyzer, and a tackle box with emergency equipment (laryngoscope, drugs, etc.).

TRANSPORT OF HIGH-RISK NEWBORN

BLACKBURN, EDWARDS, FLETCHER AND AVERY

The total cost of the equipped Infant Transport Van was between \$7,500 and \$8,000.

Principles and Practical Aspects of Transportation

Communication and teamwork are the keynotes to a successful neonatal transport system. Some details of the Children's Hospital National Medical Center's system are given, by way of example. The distance the van will travel has been set at one hour's traveling time in each direction for the most efficient use of personnel.

The initiation of transport is by request of the referring physician, and is therefore influenced by his experience and training, the local facilities and personnel, and their overall ability to cope with the problem. Whenever possible it has been the hospital policy to accept all distressed infants, providing the infant will benefit from the transport. The physician receiving the call in turn notifies the nursing staff, van driver, respiratory therapy, and the transport team of the specifics of the problem, and a plan of action is formulated. The referring physician is requested to provide a tube of clotted blood from the mother, a copy of the mother's and infant's chart, x-rays of the infant, and names and telephone numbers of himself and the parents. The referring physician should inform the parents of the reason for transfer, and ask the father to be ready to accompany the van in his own car if possible. The father can be a valuable source of information that is not available on the chart. He can also become acquainted with the physicians and nurses caring for his child, can get a better understanding of the infant's problems, and can communicate the infant's condition and progress to his wife.

Interim care of the baby is most important. The referring physician

should check the hematocrit and Dextrostix^R and give blood, albumin or glucose as indicated. If possible he should obtain blood gases and give oxygen and bicarbonate as necessary.

The transport team consists of three people, a driver and either two physicians or a physician and nurse to care for the infant. The latter two are responsible for collecting the emergency box, transport record sheet and the incubator. They also check the incubator battery and oxygen tanks prior to leaving.

At the referring hospital, the infant is stabilized before attempting transport. If there is a history of asphyxia and respiratory distress, bicarbonate, 1-2 mg per Kg, is arbitrarily given. Uncorrected hypoxia, hypoglycemia, and hypovolemia are dealt with immediately. If a large vessel is needed for infusion, the umbilical vein is used to save time. Contact is made with the parents to explain the transport and the nature of the care their infant will receive. The parents are given the telephone number of the intensive care nursery and encouraged to call or visit

as often as possible. An effort to keep in touch is also made by the receiving center, either directly or via the referring physician.

Results of Our Experience

The first infant was transported to the Children's Hospital National Medical Center on February 11, 1972, via the Infant Transport Van. Two years later, a total of 294 newborns have travelled in the van, averaging 12 babies a month. To date we have picked up infants from 16 Washington area institutions in the District, Maryland and Virginia.

Of the 294 infants transported in the first 24 months of operation, 60% (178) were transferred for respiratory distress (Table I). Twenty-three per cent (41) required ventilatory assistance during transit and all were oxygen-dependent. Two infants suffered a complete cardio-respiratory arrest en route, and were successfully resuscitated. Of the infants with respiratory distress, 91% (159) had hyaline membrane disease (HMD). The overall

TABLE I: Clinical Findings of the Transported Infants

	No.	%	% Mortality
Total number of infants	294	100	27
Diagnosis:			
Hyaline membrane disease	159	54	27
Surgical	25	9	40
Cardiac	27	9	37
Meconium aspiration	19	6	53
Infectious process	20	7	5
Miscellaneous	17	6	23
Seizures	13	4	0
Congenital anomalies	7	2	43
Jaundice	4	1	0
Neurosurgical	3	1	33
Temperature on arrival			
>36° (97° F)	218	74	
35-36°	52	18	
<35° (95° F)	24	8	

mortality for those infants with HMD was 27% (43). Fifteen weighed less than 1000 grams, and twenty-five had severe HMD. The other 19 babies transported for respiratory distress all had meconium aspiration syndrome of varying severity. Of these, 53% (10) died despite respiratory therapy.

The problems requiring transfer of the 116 remaining infants can be seen in Table I. Twenty-seven of the infants died. Of these 27, twenty had uncorrectable congenital anomalies, three had necrotizing enterocolitis, and one had Reye's syndrome.

Ninety-two per cent of the infants with HMD weighed less than 2500 grams; 43% were below 1500 grams. The mortality rate for the infants in each birth weight category can be seen in Table II. Seventy-four per cent of these infants arrived at the Children's Hospital National Medical Center nursery with rectal temperatures greater than 36°. Eighty-five per cent of the infants were transferred within the first 24 hours of life, with 75% coming before 12 hours of age (Table III).

It is somewhat difficult to quantify the impact of the infant transport system, in that there are no comparable "pre-van" statistics. However, admissions for hyaline membrane disease have doubled since the van has been in operation. The subjective opinion of the neonatology staff at Children's Hospital National Medical Center is that the infants transferred by van arrive earlier, warmer, and in better general condition than pre-van experiences. There have been no fatalities to date in transit.

TABLE II: Infants Transported Because of Hyaline Membrane Disease

Birth Weight	No.	% Mortality
<1000 grams	18	83
1000-1500 grams	50	38
1500-2000 grams	58	12
2000-2500 grams	18	one death
>2500 grams	13	one death

TABLE III: Age of Transfer of Babies with Hyaline Membrane Disease

	No.	%
0-6 hours	75	47
6-12 hours	44	28
12-18 hours	7	4
18-24 hours	8	5
24-48 hours	10	6
>48 hours	15	9

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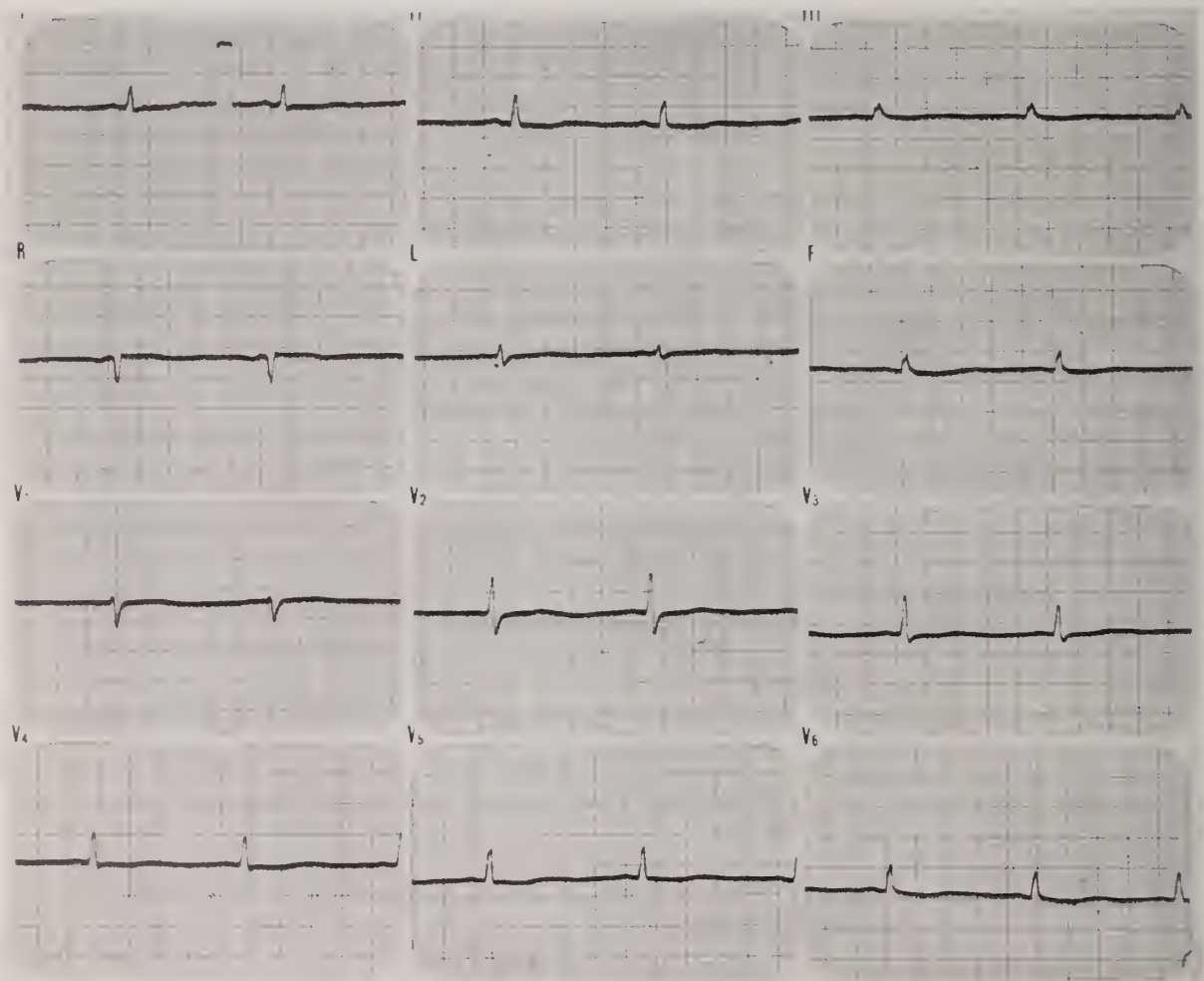
References

1. SEGAL, S.: Transfer of a premature or other high-risk newborn infant to a referral hospital. *Pediatric Clin N. Amer* 1966, 13:1195.
2. SEGAL, S., ED: *Manual for the Transport of High-Risk Newborn Infants; Principles, Policies, Equipment, Techniques*. Vancouver, Canadian Pediatric Society, 1972.
3. SWYER, P. R.: The regional organization of special care for the neonate. *Pediatric Clin N Amer* 1970, 17:761-776.

ECG PROBLEMS

HISTORY: A 50-year-old white female with long-standing history of cardiomegaly was admitted to the hospital because of progressive dyspnea and ascites. Physical examination showed a normal blood pressure, distended cervical veins, cardiac enlargement, no murmurs, and no gallop sounds.

(for diagnosis see page 358)



A Survey of Immunization Status of Children Enrolled in a Comprehensive Health Clinic

J. WM. OBERMAN, M.D.

Abstract

A neighborhood child health clinic which stresses continuity of care is one model which can encourage greater participation of young inner city children in immunization programs. There is, however, much less emphasis on determining the immunization status of the school age child.

The widespread availability in the United States of high quality vaccines against common childhood diseases—diphtheria, pertussis, tetanus, poliomyelitis, measles and rubella—resulted in a very gratifying drop in the number of cases reported annually during the 1960's. However, optimism that these diseases no longer constitute a hazard to the health of children has had to be tempered following frequent reports of "mini-epidemics" during the last several years.¹⁻⁵ In almost all instances, the victims have been preschool and elementary school children who have been unimmunized or only partly immunized.

The problem is not a small one. Almost two of every five children 1-4 years of age have no or inadequate protection against poliomyelitis and measles;⁶ one of five has not received the recommended number of DPT immunizations. The situation is par-

ticularly acute within central cities containing large poverty areas; scarcely half of the preschool children are completely immunized. And we are losing ground: the number of preschoolers adequately immunized against poliomyelitis has dropped from a high of 88% in 1964 to 63% in 1972. Katz⁵ notes that the reasons for this are complex and involve sociologic, economic, educational, political and logistical considerations.

How successful are programs designed specifically to improve the health status of inner city children in carrying out recommended immunization procedures in the population they serve? One such program is CompCare, operated by the Children's Hospital National Medical Center, under a grant from the Department of Health, Education & Welfare. For the past seven years, CompCare has operated three neighborhood clinics in center city D.C., each designed to provide continuing medical care, periodic screening for disease and ongoing health supervision to children and adolescents in the immediate surrounding community.

As part of an ongoing evaluation of the quality of care offered by CompCare, the entire registered population of children in one of its operating

Almost two of every five children 1-4 years of age have no or inadequate protection against poliomyelitis and measles; one of five has not received the recommended number of DPT immunizations. The situation is acute within central cities . . . scarcely half of the preschool children are completely immunized.

units, the Child Health Center, was surveyed for immunization status during 1972. The Child Health Center (CHC) is the smallest of the three neighborhood clinics and offers health care to children living in three census tracts of the upper Shaw area of D.C. It is atypical of most inner city health programs in several respects: it serves a small geographic area, it has a relatively small caseload and it has the additional resources of a multidisciplinary staff (nurses, social workers, neighborhood health aides) which enable maximum outreach to families of registered children. In addition, physician turnover has been minimal over a seven-year span. The CHC attaches maximum importance to systematic

IMMUNIZATION OF CHILDREN IN A COMPREHENSIVE CLINIC

OBERMAN

followup of broken appointments and encourages periodic health reassessments. The completion of an immunization series receives high priority.

The clinic has adopted the immunization schedule recommended by the American Academy of Pediatrics: an initial series of three Diphtheria Pertussis-Tetanus (DPT) at monthly and three Oral Poliomyelitis Vaccine (OPV) immunizations at bimonthly intervals during the first six months of life, starting at two months of age; measles vaccination at age one year; booster doses of DPT and OPV at 18 months of age and again in the immediate pre-school period; and rubella vaccination sometime after the first year of life—in recent months this usually has meant administering combined measles and rubella vaccines soon after 12-months of age. Some physicians preferred to give an initial immunizing series of only two bimonthly doses of oral poliomyelitis vaccine, as recommended by the Public Health Service. Levels of immunity have been shown to be comparable with either the two or three dose regimen, when a booster dose is given a year later.⁷

This survey was designed for three purposes: 1) to determine the immunization status of registered children, 2) to assess the importance placed by physicians and/or parents on complet-

ing an immunization series, and 3) to demonstrate whether or not a program emphasizing continuity of health care beyond the pre-school years results in a progressively greater percentage of children successfully immunized.

At the time of the survey, 1038 infants and children were enrolled in the CHC; 977 were 12-months of age or older, 55% of the children were boys and 45% girls; all but three were black.

A child was considered to be "active" if he or she had made at least three visits to the CHC, and at least one in the 12-months preceding the survey. Many children no longer considered active by the clinic had completed the recommended number of immunizations for their age prior to becoming inactive. Our experience indicates that many of these will continue to make sporadic visits, primarily for acute illness.

Only those immunizations recorded on the charts as having been given on a specific date were judged completed. Such comments as "up-to-date" or "given in school" were not accepted as a valid indication of a successful immunization procedure, but were assigned to the category of "no information". Numerous spot checks by ourselves and others indicate that such comments are seldom reliable; when parents do not remember they often

tell a physician what they think he wants to hear.

A number of children were regularly attending the clinic and were assigned to a category "not done—active". The assumption is that the great majority will complete the immunizations appropriate to their age. A category, "not active/no information", was developed for two groups of children: those for whom specific immunizations were not performed and who were no longer attending the clinic and those children, both in an active and inactive status, for whom no information or general information only was provided. These categories were comprised largely of school-age children.

Survey Results

The immunization status of the 977 children, 12 months of age and over, for the initial series and two booster doses of DPT; the initial series and two booster doses of OPV; and measles and rubella vaccination are presented in Tables I through III. In Table IV, those children known to be immunized and those likely to become immunized due to continuing clinic attendance ("not done—active") are combined. Additional data are provided on the per cent of children still active in each age grouping and the

TABLE I: Immunization Status, 977 Children Over 1 Year of Age Enrolled in a Comprehensive Care Clinic: DPT Vaccine

Age (yr/mos)	# of Children	Init. DPT			#1 Booster DPT			#2 Booster DPT†		
		Done	ND-A*	NA/NI*	Done	ND-A	NA/NI	Done	ND-A	NA/NI
1/0-3/11	319	292 (92%)	22 (7%)	5 (1%)	214 (67%)	81 (25%)	24 (8%)	—	—	—
4/0-5/11	165	125 (76%)	19 (12%)	21 (12%)	108 (65%)	26 (16%)	31 (19%)	36 (22%)	80 (49%)	49 (29%)
6/0-9/11	323	178 (55%)	10 (3%)	135 (42%)	152 (47%)	23 (7%)	148 (46%)	80 (25%)	67 (21%)	176 (54%)
>10/0	170	37 (22%)	1 (—)	132 (78%)	27 (16%)	5 (3%)	138 (81%)	16 (9%)	8 (5%)	146 (86%)
Total	977	632 (65%)	52 (5%)	293 (30%)	501 (51%)	135 (14%)	341 (35%)	132 (20%)	155 (24%)	371 (46%)

* ND-A: Not yet done—child still active in clinic; NA/NI: no longer active in clinic and/or no information in record.

† 685 registered children over 4 years of age.

TABLE II: Immunization Status, 977 Children Over 1 Year of Age Enrolled in a Comprehensive Care Clinic: Oral Poliovaccine

Age (yr/mos)	# of Children	Init. OPV			#1 Booster OPV			# Booster OPV†		
		Done	ND-A*	NA/N1*	Done	ND-A	NA/N1	Done	ND-A	NA/N1
1/0-3/11	319	304 (95%)	11 (4%)	4 (1%)	204 (64%)	89 (28%)	26 (8%)	—	—	—
4/0-5/11	165	133 (80%)	17 (10%)	15 (10%)	105 (64%)	29 (18%)	31 (18%)	33 (20%)	82 (50%)	50 (30%)
6/0-9/11	323	182 (56%)	7 (2%)	134 (42%)	132 (41%)	35 (11%)	156 (48%)	66 (20%)	73 (23%)	184 (57%)
>10/0	170	38 (22%)	— (—)	132 (78%)	27 (16%)	5 (3%)	138 (81%)	16 (9%)	8 (5%)	146 (86%)
Total	977	657 (67%)	35 (4%)	285 (29%)	468 (48%)	158 (16%)	351 (36%)	115 (17%)	163 (25%)	380 (58%)

† 658 registered children over 4 years of age.

* NDAA: not yet done—child still active in clinic; NA/N1: no longer active in clinic and/or no information in record.

median age at registration for clinic services.

The one to four year olds were registered by their parents in the clinic at a very young age. Almost all had completed or probably will complete their initial series of DPT and OPV, and only a slightly smaller number have been or probably will be immunized against measles. Almost two-thirds already have been immunized against rubella and had their first DPT and OPV booster. Continued clinic attendance will boost these figures to 90% or over. The great majority of children remained active in the clinic during this age period or had completed appropriate immunizations prior to becoming inactive.

Checks of clinic records confirm the inference from data in Table IV on age at registration that most of the children in the three older age groups were siblings of the one to four year olds and had received at least a portion of their immunizations elsewhere.

A disappointingly large number (30%) of four and five year olds were not actively receiving clinic services. While three quarters had completed the primary series against DPT and 80% against polio, corresponding figures for measles and rubella were 55 and 40%, respectively. About two-thirds had received their first DPT and OPV boosters, but only one-fifth their

second boosters. Since the younger sibs of many continued to attend the clinic, the four and five year olds would appear to be a high priority group to encourage completion of the immunization series.

A different sort of phenomenon was noted in the two older age groups. Most were enrolled after beginning school and the focus of physician and parent alike was on the treatment of acute illness. Data on immunization status largely was unavailable or incomplete. Physicians either had not inquired into a history of past immunizations or the mother could not remember, had lost the immunization

card, and so on. In any event, a basis was not established for a continuing relationship which could encourage completion of indicated immunizations.

Comment

Children living in inner city poverty areas consistently have immunization levels far lower than national averages. During 1971, nationwide, it was estimated that only 48.7 of these children, aged one to four years, had received measles vaccine. Comparable figures for DPT (3+ doses), OPV (3+ doses) and rubella vaccine are 58.4,

TABLE III: Immunization Status, 977 Children Over 1 Year of Age Enrolled in a Comprehensive Care Clinic: Measles & Rubella Vaccine

Age (yr/mos)	# of Children	Rubeola			Rubella		
		Done	ND-A*	NA/N1*	Done	ND-A	NA/N1
1/0-3/11	319	273 (86%)	31 (10%)	15 (4%)	201 (63%)	82 (26%)	36 (11%)
4/0-5/11	165	93 (56%)	37 (22%)	35 (22%)	65 (40%)	56 (34%)	44 (26%)
6/0-9/11	323	176 (55%)	11 (3%)	136 (42%)	103 (32%)	42 (13%)	178 (55%)
>10/0	170	36 (21%)	6 (4%)	128 (75%)	21 (12%)	12 (7%)	137 (81%)
Total	977	578 (60%)	85 (9%)	314 (31%)	390 (40%)	192 (20%)	395 (40%)

* ND-A: not yet done—child still active in clinic; NA/N1: no longer active in clinic and/or no information in record.

IMMUNIZATION OF CHILDREN IN A COMPREHENSIVE CLINIC

OBERMAN

54.3 & 52%, respectively.¹⁶ A child health center which is oriented to a specific neighborhood, emphasizes continuity of care, and has additional resources for outreach to families would appear to be one model successfully encouraging greater participation in immunization programs.

The model has not been entirely successful in overcoming the drifting away of four and five year olds from scheduled visits for health supervision, which includes the final pre-school boosters. This is a frequently observed phenomenon. In California, in 1957, 69% of one-year olds had received the recommended DPT injections, but only 32% of children in the immediate pre-school period had received their pre-school boosters.⁸ Further, in previous years, over 40% of all children reported by state health departments as having received services in a child health conference were infants, although infants comprised only one-sixth of the population.

In our own instance, almost one-third of four and five year old children were no longer considered active in the clinic, despite a clinic philosophy which emphasizes a series of pre-school screening examinations, and

frequently despite the continuing attendance of a younger sibling. The orientation of parent (and pediatrician) to the infant and younger child remains. Perhaps it can only be overcome by planned pre-school immunization drives, conducted by the clinic, analogous to those sponsored by Headstart and other organized day care facilities.

Once the child was of school age, there was little interest in clinic or parent inquiring into immunization status. In many instances the parent obviously did not know and no longer had the child's immunization card. This is not unusual: Meyer and Haggerty have found that approximately two-thirds of parents visiting a child health clinic or a hospital outpatient department with their children had not been or did not know whether they had been immunized against DPT.⁹

Needed immunizations frequently are provided as part of school health programs. But even here, there are serious gaps in information. In a small survey, conducted by the author, of five and six year olds attending first grade in a public school, 38 of 67 children had received combined

measles-rubella vaccine as part of a school immunization program, *following the obtaining of parental permission*. Cross-checking with clinic charts indicated that 16 of the 38 children previously had received immunizations against these diseases. Either the parent was not aware of her child's immunization status or had incomplete knowledge of recommended immunization practices.

A recent regulation of the D.C. City Council requires that each child admitted to school show evidence of immunization against measles, polio, tetanus and diphtheria. While this has had some effect in encouraging immunization, in practice the child will usually be allowed to attend school if the parent can show that a start has been made toward completing the series. This does not necessarily guarantee the series will be completed. In any event, it does not solve the problem of a susceptible pre-school child.

Anderson and Winkelstein question the purpose of immunization records if over the years this information is lost and unavailable to the person immunized as well as to the public health authorities.¹⁰ In the era of the

TABLE IV: Immunization Status, 977 Children Over 1 Year of Age Enrolled in a Comprehensive Care Clinic
Percent Known to be Immunized or Likely to Become Immunized

Age (yr/mos)	#of Children	% Ac- tive*	Median age at Regis- tration (yr/mos)	Init. Series DPT (%)	Init. Series OPV (%)	Measles (%)	Rubella (%)	#1 Booster DPT (%)	#1 Booster OPV (%)	#2 Booster† DPT (%)	#2 Booster† OPV (%)
1/0-3/11	319	86	<0/6	99	99	96	89	92	92	—	—
4/0-5/11	165	70	3/1	88	90	78	74	81	82	70	71
6/0-9/11	323	50	5/2	58	58	58	45	54	52	43	46
>10/0	170	50	7/6	22	22	25	33	19	19	14	14

† 658 registered children over 4 years of age.

* Active: at least 3 clinic visits, one during the preceding year.

computer it would not seem difficult to devise a system to collect at one location data on the immunization status of each individual. The cost of such a program would be more than offset by the amount of professional time wasted in obtaining this information.

References

1. MILLER, L. W., OLDER, J. J., DRAKE, J., ZIMMERMAN, S.: "Diphtheria Immunization, Effect Upon Carriers & the Control of Outbreaks", *Amer. Journ. Dis. Children* 1972, 123:197.
2. CHERRY, J., FEIGIN, R., LOBES, L., HINTHORN, D., SHACKELFORD, P., SHIRLEY, R., LINS, R., CHOI, S.: "Urban Measles in the Vaccine Era. A Clinical, Epidemiologic & Serologic Study," *Journ. Pediatrics* 1972, 81:217.
3. MELNICK, J., BURKHARDT, M., TABER, L., ERCKMAN, P.: "Developing Gap in Immunity to Poliomyelitis in an Urban Area", *J.A.M.A.* 1969, 209:1181.
4. "Pertussis Thrives on Poverty", *Medical World News*, June 26, 1970, p. 20.
5. KATZ, S. L.: "Commentary: Immunization Action Month, October, 1973", *Pediatrics* 1973, 52:483.
6. *Immunization Against Disease: 1972*, U.S. Dept. HEW, Center for Disease Control, Atlanta, pp. 76-77.
7. HARDY, G. E., HOPKINS, C. C., LINNEMANN, C. C., HATCH, M. H., CHAMBERS, J. C., WITTE, J. J.: "Trivalent Oral Poliovirus Vaccine: A Comparison of Two Infant Immunization Schedules", *Pediatrics* 1970, 45:444.
8. LESSER, A.: "Health of Children of School Age", U.S. Dept. HEW, Children's Bureau #427-1964, pp. 14-15.
9. MEYER, R. J., HAGGERTY, R. J.: "The Immunization & Tuberculin-Testing Status of Certain Selected Families", *New Eng. Journ. Med.* 1961, 264:344.
10. ANDERSON, U., WINKELSTEIN, W.: "Immunization Status of School Children in Buffalo, N.Y., 1953 & 1963", *Amer. Journ. Pub. Health* 1966, 81:755.

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VIEW BOX

(from page 348)

DIAGNOSIS: RUPTURED ESOPHAGUS

Film #1 shows a nasogastric tube and a right subclavian line to be positioned satisfactorily. There is a left-sided pleural effusion with mediastinal air and supraclavical and nuchal subcutaneous emphysema.

Film #2 shows water soluble contrast material to have been administered with gross left-sided extravasation demonstrated. The diagnosis of ruptured esophagus was confirmed.

Ruptured esophagus leading to acute mediastinitis is often caused by excessive vomiting, most often seen in the alcoholic. Other causes of perforated esophagus include primary carcinoma, esophagoscopy, (especially with biopsy) and impacted foreign body. There is often retrosternal pain and a Hamman's crunch as in this classic case (due to soft tissue emphysema). If not recognized, a esophagopleural fistula may develop which can be demonstrated with contrast agents.

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ECG PROBLEMS

(from page 352)

INTERPRETATION:

1. Low voltage.
2. ST-T wave changes which are consistent with digitalis effect or myocardial ischemia.

The QRS complexes are small, satisfying the criteria for low voltage. In the seventh edition of the Nomenclature and Criteria for Diagnosis of Diseases of the Heart and Great Vessels of the New York Heart Association, those criteria are listed as "the amplitude of the whole QRS complex is 5 mm. or less in all six limb leads." The older edition of this work also included the requirement that the QRS amplitude in the chest leads be less than 15 mm. to establish the diagnosis of low voltage. This criterion is also met. This patient had massive pericardial effusion which was apparently chronic. A total of between 3,500 and 4,000 cc. of clear serous fluid was removed with prompt relief of her symptoms. The ST segment abnormalities disappeared as digitalis was discontinued.

*Edited by
Robert R. Montgomery, M.D.*

Use of the High Plus Bausch and Lomb Soflens[®] in the Management of Aphakia in Infants and Children

DAVID S. FRIENDLY, M.D., BLACKWELL S. BRUNER, M.D., THOMAS FREY, M.D., MARTIN E. LEDERMAN, M.D., MARSHALL M. PARKS, M.D., AND NEVIN OLDT

Abstract

Twenty-three pediatric patients representing 30 aphakic eyes were fitted with Bausch and Lomb high plus soft contact lenses. The lens was well tolerated by the patients and when not worn overnight did not produce significant corneal epithelial damage. The disadvantages encountered included occasional poor lens centering, a significant replacement rate for lost and damaged lenses and parental difficulty in discerning the lens on the eye. The problem encountered most frequently was difficulty in inserting the lens through the palpebral apertures of some young patients.

Introduction

Three methods are presently available for the optical rehabilitation of eyes following cataract surgery. For older children and adults, glasses may be prescribed. Forward lenses, however, are an imperfect optical solution to aphakia because of alterations in the peripheral field of vision, induced distortions and aberrations as well as

The main disadvantage of soft contact lenses experienced during the study was difficulty in lens insertion in young patients. Infants have the greatest need for immediate optical correction following lens surgery and frustratingly it is just this age group that is most difficult to fit.

an increase in the retinal image size. Furthermore, spectacles cannot be easily worn by infants or by many young children. Intraocular lenses have been employed by some investigators with varying degrees of success. However, the use of such lenses in growing eyes with changing refractive errors must be considered highly experimental. Experience with intraocular lenses is largely limited to adults. Their use in patients with significantly greater life expectancies necessitates studies with observations extending over more years than are presently available.

Contact lenses provide relatively good peripheral vision and produce far

fewer prismatic effects than glasses. They can be worn by infants and young children and may be replaced if power adjustments become necessary. The increase in retinal image size is significantly less than that with forward lenses. There is, therefore, little question that at the present time contact lenses are the devices of choice for the optical rehabilitation of aphakic eyes of infants and young children. Hard contact lenses have been used to correct aphakia by some of the authors of this paper for over fifteen years. The advent of high plus soft contact lenses has prompted an appraisal of their possible usefulness for this condition in the pediatric age group.

The development in 1960 by Drs. Otto Wichterle and Drahoslav Lim¹ of the Institute of Macromolecular Chemistry, in Prague, Czechoslovakia of a new hydrophilic substance-hydroxyethylmethacrylate (HEMA) led to the manufacture of a radically new type of contact lens, the hydrogel soft contact lens. The lens, which is composed of a hydrophilic polymer of HEMA, was introduced in Czechoslovakia but did

USE OF SOFT CONTACT LENSES IN APHAKIA IN INFANTS AND CHILDREN

FRIENDLY, BRUNER, FREY, LEDERMAN, PARKS AND OLDT

not at first achieve widespread acceptance elsewhere. In 1966, the Bausch and Lomb Company, under license, began to manufacture and clinically evaluate the new lens. In 1971 the Food and Drug Administration released the Bausch and Lomb Soflens® for domestic marketing. It remains today the only soft contact lens approved by the Food and Drug Administration for the correction of refractive errors. In May of 1972 the Bausch and Lomb high plus series for the correction of aphakia became commercially available.

The Bausch and Lomb soft contact lens is spincast rather than lathecut. Polymerization takes place within a spinning mold. The curvature of the convex front surface of the lens is determined by the shape of the mold; but the curvature of the back concave surface is determined by such factors as the speed of rotation, the rate of polymerization and the viscosity and temperature of the material. The curvature of the back surface is aspheric.

The Bausch and Lomb soft contact lens absorbs 38.6% normal saline by weight. The dry lens is rigid and brittle; the hydrated lens is soft and flexible and assumes its normal shape regardless of previous deformations. The polymer is biologically inert and impervious to bacteria and viruses.

Material, Methods and Results

Only Bausch and Lomb high plus soft contact lenses were used in the study. The contact lenses, which were supplied by the manufacturer, ranged in power from +9.00 to +19.50 Diopters in 0.50 Diopter steps. Lens diameters were uniformly 13.5 mm, and central thicknesses varied from 0.17 to 0.4 mm. The peripheral bevel was 0.75 mm wide. The front or convex surfaces of the Bausch and Lomb high plus soft contact lenses have a fixed radius of curvature which is 6.41 mm

for the lenticular bowl and 8.29 mm for the minus carrier. The size of the lenticular bowl is 7.9 mm. The posterior or concave surfaces vary from 7.0 to 8.2 mm, with the higher plus lenses having a flatter radius of curvature.

To have their children entered in the prospective study, parents had to be willing to attend the clinic at specified intervals. Details of the protocol were explained to the parents by the authors, and an informed consent was obtained for each patient. All eye surgery was performed by the Hospital Staff physicians. Postoperative patients were fitted for soft contact lenses following discontinuation of topical medications. The interval between lens surgery and initial soft contact lens fitting varied from one month to two years. The study was conducted over a 15 month interval, after which the results were analyzed.

Sixteen male patients and seven female patients were included in the study. Eighteen patients were referred from private physicians; five clinic patients were referred by residents and fellows in training. This ratio of private to clinic patients is similar to that of private to clinic patients that undergo general eye surgery at the Children's Hospital National Medical Center.

Seven patients received contact lenses for bilateral aphakia. Thus, the 23 patients included in the study represented 30 fitted aphakic eyes.

As shown in Table, nine patients (1-9) had bilateral cataracts. Eight of the nine patients had congenital or early infantile cataracts; one patient (1) developed bilateral cataracts during adolescence. The parents of one child (8) were unable to insert and remove a soft contact lens given for one eye. Therefore, this patient did not receive a soft contact lens for the other aphakic eye. A Mongoloid child (9) presented with highly asymmetric bilateral cataracts. Only the more

severely affected eye was operated upon and fitted with a soft contact lens. The other eight patients with bilateral cataracts had lens surgery on both eyes. Eight patients (10-17) were fitted following lens aspirations for nontraumatic monocular cataracts. Four of these eight patients had unilateral congenital or early infantile cataracts (10-13); one of these patients had an associated microcornea and probable microphthalmus (12). The other four patients in this group had unilateral posterior lenticonus (14-17). Six patients (18-23) received soft contact lenses following surgery for monocular traumatic cataracts. Two of the patients in this group (18-19) had corneal scars associated with penetrating injuries.

Three patients (3, 5 and 23) had worn hard contact lenses previously. One of these patients (3), was accepted for soft contact lenses in the expectation that a lower rate of lens loss and a less frequent need for lens removal would permit attendance at an out-of-town school. A second patient (5) was accepted for soft contact lenses because of a high rate of hard contact lens loss. The third patient (23) was fitted for a soft contact lens because previously worn hard contact lenses had produced discomfort and were not regularly being used. No successfully treated hard contact lens wearers were transferred to soft contact lenses.

The power of the contact lenses dispensed was estimated from the retinoscopic findings adjusted to zero vertex distance. Additional plus lens power was utilized when aphakic eyes of infants and young children were corrected. Infants less than 18 months of age were given +2.50 Diopters of overcorrection. Children between one and one-half and three years of age were given +2.00 Diopters of overcorrection. Patients over three years of age were not overcorrected. A trial and

TABLE

Patient	Condition	Referral source	Age at soft lens fitting		Months of wear		Number of soft lenses dispensed		Best visual acuity with soft lenses		Comments
			OD	OS	OD	OS	OD	OS	OD	OS	
1	Bilateral Acquired Cataracts	private	18 yrs	18 yrs	10	15	3	4	20/25	20/20	
2	Bilateral Congenital Cataracts	clinic	10 yrs	10 yrs	0	0	1	1	Not recorded		Unable to keep clinic appointments
3	Bilateral Congenital Cataracts, Severe Cerebral Palsy and Nystagmus	private	10 yrs	10 yrs	1	1	1	1			Previously wore hard lenses. Refused to open eyes while wearing soft lenses
4	Bilateral Congenital Cataracts and Iris Colobomas	private	8 mo	8 mo	5	5	4	2	Good fixation	Good fixation	
5	Bilateral Congenital Cataracts	private	3 yrs	3 yrs	5	5	3	4	Good fixation	Good fixation	Previously lost many hard lenses
6	Bilateral Congenital Cataracts	private	7 mo	7 mo	2	2	1	2	Fair fixation	Fair fixation	Poor blinking and poor centering of soft lenses. Transferred to hard lenses
7	Bilateral Congenital Cataracts	private	1 yr	1 yr	6	6	3	6	Fair fixation	Fair fixation	
8	Bilateral Congenital Cataracts	clinic		3 yrs		0		1		Good fixation	Parents unable to insert lens
9	Bilateral Congenital Cataracts, Down's Syndrome and Nystagmus	clinic		2 yrs		0		1		Poor fixation	Parents unable to insert lens
10	Unilateral Congenital Cataract and Nystagmus	private		8 mo		3		1		Poor fixation	
11	Unilateral Congenital Cataract	private	4 yrs		9		5		20/200		
12	Unilateral Congenital Cataract and Microcornea	private		1 yr		8		2		Poor fixation	Poor lens centering
13	Unilateral Congenital Cataracts	private	1 yr		8		5		Good fixation		
14	Posterior Lenticonus	private		6 yrs		10		3		20/200	
15	Posterior Lenticonus	private	2 yrs		0		1		Good fixation		Parents unable to insert lens
16	Posterior Lenticonus	private	2 yrs		14		4		5/200		
17	Posterior Lenticonus	private		3 yrs		6		6		20/400	
18	Traumatic Cataract and Corneal Scar	clinic		5 yrs		4		3		5/200	

USE OF SOFT CONTACT LENSES IN APHAKIA IN INFANTS AND CHILDREN

FRIENDLY, BRUNER, FREY, LEDERMAN, PARKS AND OLDT

TABLE (Continued)

Patient	Condition	Referral source	Age at soft lens fitting		Months of wear		Number of soft lenses dispensed		Best visual acuity with soft lenses		Comments
			OD	OS	OD	OS	OD	OS	OD	OS	
19	Traumatic Cataract and Corneal Scar	private	6 yrs				3	1		2/200	Had penetrating corneal graft
20	Traumatic Cataract	private		6 yrs		10		3		20/200	
21	Traumatic Cataract	clinic		4 yrs		0		1		Fair Fixation	Parents unable to insert lens
22	Traumatic Cataract	private	3 yrs		3		2		Poor fixation		Lost to follow-up
23	Traumatic Cataract	private	17 yrs		6		1		20/40		Previously wore hard lenses. Wears soft lenses infrequently. Prefers glasses which correct myopia of OS

error procedure was used to determine the lens power that provided the best centering and refractive effect. Power adjustments were made during the study whenever retinoscopic overrefractions significantly departed from desired values. The available lens powers were satisfactory for all but two patients. One patient (18) would have benefitted from a lens weaker than +9.00 Diopters and one patient (12) would have benefitted from a lens stronger than +19.50 Diopters.

The parents were given detailed instructions and repeated demonstrations in insertion and removal technique, as well as in the manufacturer's recommended method of lens care. Patients were not given soft contact lenses until the physician was satisfied that the parents thoroughly understood the procedures to be followed at home and were capable of inserting and removing the contact lenses without undue trauma or difficulty. Except as noted below, lenses were routinely removed at night, sterilized in the unit provided by the manufac-

turer, and not handled until needed the following day.

The initial intention of the investigators was to place all patients on immediate, continuous (24 hours/day) soft contact lens wear. The case histories of the first three patients (1, 15, and 16) so fitted have been previously reported² and will not be repeated in detail here. All three patients had pain, bulbar conjunctival injection and epithelial corneal edema after 24 or 48 hours of continuous wear. After removal of the lens and application of modified pressure dressings, healing in all cases was complete and without visible sequelae in 48 hours.

This early unfavorable experience suggested the use of a wearing schedule which would provide gradual increments of lens wear during the day. Accordingly, wearing time was gradually increased from three hours to 12 hours over a period of two weeks. Lenses were not worn at night or for more than two hours during day-time sleep.

Patients were examined after two days of wear, after one week of wear and after two weeks of wear. Visits were then scheduled once each month until the study was terminated. One of the authors (D.S.F.) personally examined each patient and was directly involved in the care of each patient.

The following determinations and observations were made at regular intervals during the study: visual acuities, overrefractions, external and funduscopic examinations, and keratometer measurements. Additionally, cultures for bacterial growth and identification were obtained from both eyes of each patient during the first several months of lens wear.

All patients fitted with soft contact lenses following monocular cataract surgery received occlusion therapy. Parents were generally instructed to patch the phakic eye whenever the soft contact lens was worn. Older children received supplemental reading glasses to improve vision at near fixation distances. No patients were given glasses for correction of residual

astigmatism. Soft contact lenses and patches were removed several days prior to intraocular surgery for secondary membranes.

Visual acuities with the soft contact lenses varied from 20/20 to poor fixation (see Table). It is apparent that many patients included in the study were too young to provide a meaningful assessment of visual function.

Excluding patients fitted for continuous wear, corneal staining with fluorescein dye was noted in only a few patients and was not considered significant in any of the patients. Corneal neovascularization was not encountered. Protein deposits did not develop on any of the soft contact lenses used in the study.

Keratometer measurements were obtained on all but four patients. Readings on infants and young children were obtained in the operating room with the patients under general anesthesia; readings on older children were obtained in the clinic. The mean measurement for 13 patients, representing 18 eyes, with congenital cataracts, including cases of posterior lenticonus, was 44.79 Diopters. The range of the powers of the principal meridians of the cornea of these eyes was 42.00 Diopters to 49.25 Diopters. The mean measurement for six patients, representing seven eyes, with acquired cataracts was 43.24 Diopters. The range of the powers of the principal meridians of the corneas of these eyes was 39.00 Diopters to 47.75 Diopters.

Two hundred and six eye cultures were obtained from the 23 patients included in the study. Bacteria failed to grow in 129 of these cultures. *Staphylococcus epidermidis* was the organism most frequently isolated from the 77 positive cultures. *Staphylococcus aureus* was identified in 13 cultures. However, there were no clinically evident eye infections during the course of the study.

The average patient follow-up was five months. A total of 76 lenses was dispensed for the 30 eyes fitted. Eleven soft contact lenses were replaced for power adjustments; 23 lenses were required to replace lost lenses; and 12 lenses were required to replace damaged lenses. Excluding lenses exchanged for power adjustments, on the average 0.40 lenses were required per eye per month. The replacement rate (excluding power adjustments) was 0.24 lenses per month per eye or 2.9 lenses per year per eye.

Only one patient (22) was lost to follow-up. Seven additional patients (2, 3, 6, 8, 9, 15, and 21), however, were classified as treatment failures because soft contact lens wear had to be discontinued. The parents of one patient (2) were unable to arrange clinic visits at the required intervals. One patient (3) with severe cerebral palsy refused to open his eyes after lens insertion.

One patient (6) was transferred to hard contact lenses because of persistent and severe bilateral temporal decentration. This patient blinked infrequently and the lenses appeared dry in situ. The most frequent reason for treatment failure was inability of the parents to insert the soft contact lenses. Four patients (8, 9, 15, and 21) were discontinued for this reason.

Discussion

It has been demonstrated in kittens and monkeys that visual deprivation early in life of one eye leads to atrophy of the corresponding cells of the lateral geniculate body and in kittens such deprivation leads to a marked decrease in the number of striate cortical cells that can be driven by the deprived eye³. The period of maximum susceptibility to visual deprivation for kittens and monkeys appears to be the first three months of

life. Moreover, when formed vision is prevented during this period by unilateral lid closure or by translucent occluders, the induced amblyopia is to a large extent irreversible. The existence of a similar critical period of susceptibility to visual deprivation in man is assumed from clinical observations. Its exact duration is not known, but case studies suggest that it extends over the first several years of life.

With the use of modern anesthetic and surgical techniques, the aspiration of infantile cataracts has become a relatively safe and effective procedure⁴. Although secondary membranes occur in 40 to 50% of the cases operated upon at the Children's Hospital National Medical Center, a satisfactory pupillary opening can almost always be obtained by incising the opaque retropupillary tissue. Two operations are sufficient in the vast majority of cases to obtain a clear central opening. However, visual results following monocular cataract surgery fall far short of the generally satisfactory anatomic results. Deprivation amblyopia (*amblyopia ex anopsia*) is the primary reason for therapeutic failure in such cases. Amblyopia also occurs following bilateral cataract surgery, but it tends to be less severe than in the monocular cases. Patients with traumatic cataracts and other forms of acquired cataracts have much better visual prognoses because of the absence of *amblyopia ex anopsia* prior to the onset of lens opacification⁵.

Mammalian animal experiments suggest that monocular congenital cataracts should be operated upon during the first few months of life in order to provide the best possible opportunity for monocular and binocular visual development. To prevent amblyopia from the simultaneous presence of significantly different refractive errors (anisometropic amblyopia), it is desirable to produce sharp retinal images as soon as possible after lens surgery on

USE OF SOFT CONTACT LENSES IN APHAKIA IN INFANTS AND CHILDREN

FRIENDLY, BRUNER, FREY, LEDERMAN, PARKS AND OLDT

pediatric patients with either unilateral or bilateral cataracts. Prolonged periods of uncorrected aphakia in infants and young children are undoubtedly detrimental and should be avoided whenever possible.

For the above physiologic reasons, it would be advantageous to place a contact lens on aphakic eyes of infants and young children immediately after lens surgery. For practical reasons it would be desirable in such cases to leave the lens on the eye and not remove it except for periodic inspection, cleaning and power adjustment.

Lens fittings were not attempted during the immediate postoperative period in this study, because it was thought advisable to postpone manipulation of the eye until inflammation had subsided and the surgical wound had partially healed. There was also some reluctance to instill medications with the lens in situ because of its absorbant properties which would result in sustained release of drugs and preservatives.

The feasibility of continuous soft contact lens wear was tested on three patients. The severe epithelial edema produced in each of these patients did not encourage further experimentation along these lines. Nevertheless, the possibility could not be eliminated that the corneal epithelium might be better able to withstand the induced hypoxia if first given an opportunity to adjust to lower oxygen partial pressures. Therefore, overnight wear was allowed in one (#16) of these three patients after three months of successful day-time wear. The edema and discomfort recurred after 24 hours of continuous wear despite the prolonged period of adaptation. Patient (5) after four months of successful day-time soft contact lens wear inadvertently wore a soft contact lens for two consecutive nights because the patient's mother thought the lens was lost and did not realize it was still on

the patient's eye. This patient awoke after the second night of continuous wear with severe ocular pain. Examination revealed a large area of denuded corneal epithelium that stained with fluorescein dye (see photograph). In this patient, as well as others, the most severely affected epithelium was that portion covered by the thick lenticular bowl of the soft contact lenses. For hydrogel lenses it has been shown that within a ten percent range of hydration, lens thickness is the single most important variable influencing corneal physiology⁶. In the closed eye, oxygen diffusion fluxes through the soft contact lenses employed were inadequate to satisfy the respiratory requirements of the corneal epithelium⁷.

The above clinical observations, as well as those of others⁸, would suggest considerable caution in attempting continuous wear of high plus soft contact lenses on aphakic eyes. Reports of occasional patients that have

successfully worn such lenses on a continuous basis have come to our attention^{9,10}. The factors permitting success in such cases are not clear but may relate to relative lens thickness, to the rate and volume of fluid exchange between the lens and the corneal epithelium and to the extent and duration of lid closure.

Except when worn overnight, the soft contact lenses caused little or no visible corneal epithelial damage. Slight peripheral punctate staining with fluorescein dye was occasionally noted on slit lamp examination. This was thought to be of no clinical significance and certainly no more marked than that taking place after equal periods of hard contact lens wear. The soft contact lenses were well tolerated, and the older children reported that they experienced no discomfort while wearing the lenses. Patient (23) did not wear soft contact lenses consistently, but the rea-



The right eye of patient #5 after 48 hours of continuous soft contact lens wear. The light appearing central corneal area represents an epithelial defect stained with fluorescein dye.

sons were not related to lens comfort. The parents did not find the cleaning or sterilizing techniques arduous.

The inability of soft contact lenses to neutralize significant corneal astigmatism was noticed in several patients. However, the reduced visual acuity as a result of residual astigmatism was insignificant compared to the reductions in acuity from both anisometropic amblyopia and amblyopia ex anopsia. Therefore, spectacles were not prescribed except to permit visual activities at near working distances.

The posterior curves of the Bausch and Lomb high plus soft contact lenses become flatter with increasing lens powers. This characteristic may necessitate a compromise between good centering and proper refractive power. Centering difficulties were encountered in two of the patients of the present series. In patient (6) it was necessary to substitute hard lenses for the soft lenses in order to obtain a reasonable fit. In patient (12) with microcornea, the lens tended to ride high; only the peripheral portion of the lenticular bowl covered the pupillary opening.

A rather high rate of soft contact lens replacement for power adjustments, lens loss and lens damage was encountered. With greater experience on the part of both physicians and patients, this replacement rate will undoubtedly decrease. Nevertheless, it is of interest that in a comparable age group of 25 patients representing 31 aphakic eyes fitted with hard lenticular lenses, the replacement rate, excluding power adjustments, was 0.16 lenses per month per eye or 1.9 lenses per year per eye. This is a lower rate than was found with the soft contact lenses.

The rate of contact lens loss (both hard and soft) appears to be age related with the highest rates occurring in the youngest patients. The single patient (#5) that was observed for several months following a transfer

from hard to soft contact lenses because of a high rate of hard lens loss, continued to lose soft lenses at a high rate.

Many parents complained of difficulty in discerning the lens on their child's eye. The edge of the soft contact lens and the edge of the lenticular bowl could invariably be identified by the attending physicians in the clinic. In the home environment, however, with less than optimum illumination, restraint of the patient, and exposure of the cornea, it would be difficult at times to determine whether or not the lens was actually on the eye. As previously mentioned, on one occasion a lens was inadvertently worn for two consecutive nights because the patient's mother was unable to verify visually the presence of the lens on her child's eye and believed it had fallen out. Contrary to oral instructions, parents failed on several occasions to confirm visually the presence of the lens on the eye prior to lens removal while demonstrating removal technique to the attending physician in the clinic. Despite this apparent laxity, corneal abrasions from fingers and fingernails were not observed during the course of the study.

The main disadvantage of soft contact lenses experienced during the study was difficulty in lens insertion in young patients. Infants have the greatest need for immediate optical correction following lens surgery and frustratingly it is just this age group that is most difficult to fit. The problem is entirely mechanical in nature. The palpebral apertures of some of the young patients included in the study were simply too small to admit readily the 13.5 mm diameter lenses. Three adults were at times required to place lenses on the eyes of infants. One was required to restrain the patient's head, a second to separate the eyelids and a third to introduce the soft contact

lens. Folding the lens so that its long axis was parallel to the lid margins was found to be helpful. Even with the aid of this maneuver, in some cases lens insertion was still very difficult primarily because of the inability of some parents to retract the eyelids sufficiently to introduce the lens.

The difficulties with soft contact lens insertion experienced in some of the patients included in this report were apparently not encountered in a previous study¹¹ dealing with similar subjects and material. The reasons for this discrepancy are not apparent. Inability to insert the soft contact lenses accounted for four of the eight therapeutic failures that occurred during the course of the study. The parents involved lacked the physical ability, psychological resolve or the necessary assistance to comply with the fitting instructions. Removal of the soft contact lenses, on the other hand, was a relatively simple procedure that did not cause difficulty for any of the parents.

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References

1. WICHTERLE, O., LIM, D.: Hydrophilic gels for biological use. *Nature* 1960, 185:117-118.
2. FRIENDLY, D. S., Bruner, B. S., FREY, T., LEDERMAN, M. E., PARKS, M. M., OLDT, N.: Continuous wear of soft contact lenses. *Archives of Ophthalmology* 1973, 90:343-344.
3. WIESEL, T. N.: Effects of monocular deprivation on the cat's visual cortex. *Transactions of the American Academy of Ophthalmology and Otolaryngology* 1971, 75:1186-1192.
4. PARKS, M. M., HILES, D. A.: Management of infantile cataracts. *American Journal of Ophthalmology* 1967, 63: 10-19.

USE OF SOFT CONTACT LENSES IN APHAKIA IN INFANTS AND CHILDREN

FRIENDLY, BRUNER, FRAY, LEDERMAN, PARKS AND OLDT

5. FREY, T., FRIENDLY, D., WYATT, D.: Re-evaluation of monocular cataracts in children. *American Journal of Ophthalmology* 1973, 76:381-388.
6. KORB, D. R., REFOJO, M. F., CONNOLLY, E. B., AHMAD, B.: Thickness and transparency of the cornea while wearing hydrogel contact lenses of varying thicknesses: clinical and academic considerations. Submitted for publication. *International Contact Lens Council of Ophthalmology*.
7. HOLLY, F. J., REFOJO, M. F.: Oxygen permeability of hydrogel contact lenses. *Journal of the American Optometric Association* 1972, 43:1173-1180.
8. BLACK, C. J.: The continuous wear of the Bausch and Lomb Soflens for aphakic correction. *The Contact Lens Medical Bulletin* 1973, 6:37.
9. CLAHR, L.: Continuous wear of soft contact lenses by aphakic patients. *The Contact Lens Medical Bulletin* 1973, 6:35-36.
10. DYER, J.: The Contact Lens Medical Bulletin. Discussion of Enoch, J. M.: The fitting of hydrophilic (soft) contact lenses to infants and young children II. *The Contact Lens Medical Bulletin* 1972, 5:48-49.
11. ENOCH, J. M.: The fitting of hydrophilic (soft) contact lenses to infants and young children II. *The Contact Lens Medical Bulletin* 1972, 5:41-47.

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SPECIAL ARTICLE

Acupuncture for Deafness: A Study of Patients Treated in Washington, D.C.

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Abstract

Of the many unproven remedies for nerve deafness, few have flourished so suddenly or so captured the public attention through the national news-media as has acupuncture. Most reports have been anecdotal, defying verification. This retrospective study reviewed audiograms before and after acupuncture on 121 ears of 64 patients who had undergone treatment in Washington, D.C. for hearing impairment. None of the patients showed significant improvement in averaged pure tone thresholds. None showed improvement in speech reception thresholds. Speech discrimination was similarly unaffected except for a few isolated instances. Unfortunately, the number of patients showing possible improvement was offset by a number twice as large who showed deterioration. Testing artifact and disease progression are both possible. These data do not support the popularized notion that acupuncture cures deafness.

The purpose of this report is to document with analysis of pre- and post-treatment audiograms the efficacy or non-efficacy of acupuncture for treatment of nerve deafness, as practiced in the Washington, D.C. area. This study was undertaken at the request of the Otolaryngology Section

This retrospective study reviewed audiograms before and after acupuncture on . . . patients who had undergone treatment in Washington, D.C. for hearing impairment. . . . none showed significant improvement

of the Medical Society of the District of Columbia.

Introduction

Many remedies have been proposed for treatment of neurosensory hearing loss, yet few have so captured the public attention as acupuncture. In 1972, a noted American otologist returned from his tour of mainland China and commented on the ancient art of acupuncture to *Newsweek* reporters: "My colleagues and I have seen the past, and it works." However, Okamoto, (Chairman, Dept. of Otolaryngology, Showa University, Tokyo) also took a fact-finding trip to China and found little or no evidence that acupuncture cured a sensorineural

hearing loss. Furthermore, he met no one in China who knew how to obtain an audiogram. (Private communication with H. Shimizu, available on request from American Council of Otolaryngology.) In 1970 an oriental acupuncturist offered his services to the Federation School for the Deaf in Penang, Malasia. Audiometric tests were conducted on twenty-eight children before and after acupuncture treatments. None were cured or significantly improved. (Private communication by S. Yahaya-Isa, available on request from American Council of Otolaryngology.)

Never-the-less, the practice spread to the United States, and experienced a most phenomenal surge following a series of national wire service news releases which prompted headlines such as: "Acupuncture Cures Nerve Deafness For Floridian," "Needles Open New Worlds" and "Acupuncture Holds New Hope For Nerve Deaf."¹ Readers were led to believe that improvement in hearing was medically accepted in numerous cases, when—in fact—the scientific community has not been made privy to any such information.

An intensive literature survey uncovered only four articles in medical journals in the English language where the subject had been discussed.^{2,3,4,5} Only two of these articles include

ACUPUNCTURE FOR DEAFNESS

FAIRBANKS, WALLEMBERG AND WEBB

audiometric studies. They are admitted by their authors to be preliminary reports and their conclusions are generous and non-critical.

Particular attention should be paid to the article by Peng³ of "Columbia University" because it has been so widely quoted by the acupuncture community as documenting an 80% success rate in treating deafness. However, only one of Peng's ten reported cases is presented with pre- and post-acupuncture audiograms. The tests were done by techniques clearly not comparable to each other; the audiometers were calibrated to differing standards. No notations are made as to dates of testing, masking, or speech testing. In the text he appears to have considered 80 *per cent* loss the same as 80 *decibel* loss (an error reflecting either gross indifference to accuracy or lack of comprehension). That report must be considered void of scientific merit.

Present U. S. laws allow non-M.D. acupuncturists to practice only in a few states and the District of Columbia. Most of the popular attention to acupuncture for hearing loss has focused on centers in Washington, D.C., where there are at least twelve with more soon to open. One of them processes up to 100 patients per day, 90% of whom are seeking a cure for deafness. Patients come from widely scattered parts of the United States. Travel and housing in local hotels are major expenses. One center reserves hotel rooms for its patients in one location and provides a limousine shuttle to and from the clinic. Soliciting techniques include lectures to lay groups, "news releases" to the popular press, and, most recently, paid television advertisements. At least one of the centers employs a Washington based public relations firm.

Washington acupuncturists exhibit considerable individuality in technique. Treatment uses two to six



Fig. 1. Acupuncture for deafness consists of two to six needles inserted around the ear. They may be twirled, heated or electrically stimulated. Distant puncture sites in the scalp and extremities are also thought to be important in some patients.

needles around the pinna (see Fig. 1), sometimes supplemented by needles in the coronal scalp, hands, wrists and feet. Needles are left in place about thirty minutes and may or may not require twirling. Low voltage electrical stimulation through the needles is an embellishment promoted at one center; another gives heat treatments ("Indirect Moxa") to the puncture sites after needle removal.

Treatments cost up to \$50 for the initial visit and \$35 for subsequent ones. The protocol varies between centers but ten treatments is the usual initial recommendation for a daily or alternate day regimen. Patients who are "cured" by this need only to return for booster treatments as needed. However, those who get only partial (or no) improvement are urged to return for another ten treatments by a different technique or at an interval one month later. Patients who

fail to respond to twenty treatments are allowed to terminate therapy, but the suggestion is often made that in China they continue treatments even longer than a year.

Many patients choose not to complete the course, whether for disillusionment, pain (especially in children), or cost. Said the director of one large center, "They just run out of money."

Method

Audiologists, otolaryngologists and other workers with the deaf in the Washington-Baltimore area were requested to retrieve all audiometric studies they had performed on patients who had undergone acupuncture for deafness in any of the Washington, D.C. centers. Responses were obtained from eighteen individuals or institutions. Audiograms on sixty six patients were received, documenting the mea-

surable hearing before and after acupuncture treatments. Individual data on each patient are available on request from the authors. The pure tone thresholds represented are the averages of responses at .5K, 1K, and 2K H_z except when responses were not obtainable at those frequencies. In such instances whatever frequencies were testable were utilized.

All post-treatment audiograms were performed in the latter part of 1973. Pre-treatment audiograms were all performed within a few months prior to treatment with the exception of thirteen cases. Eleven of these were within the last three years; their results were not substantially different from those tested in 1973, so they were included in the study. However, two patients had pre-treatment audiograms in 1965. These were omitted from the study because eight year interval between pre- and post-treatment audiograms was considered inappropriate for comparative purposes.

Pre- and post-treatment audiograms were performed in the same testing environment with the exception of three cases. Whenever testing techniques were not comparable the results were omitted from the summary tables.

Results

This study contains the problems inherent in retrospective investigations; the data do not conform to a pre-determined protocol, and some informational items are absent. Calibration and standardization of equipment or testing techniques are not considered in this survey, since the issue under study is the difference in—rather than the absolute level of—hearing before and after acupuncture. The validity of these comparisons is emphasized by the fact that pre- and post-treatment audiograms were performed in the same testing environ-

ment (except as noted). Audiological studies were performed under the direction of qualified otolaryngologists and audiologists who are held in high esteem in their local and national professional communities.

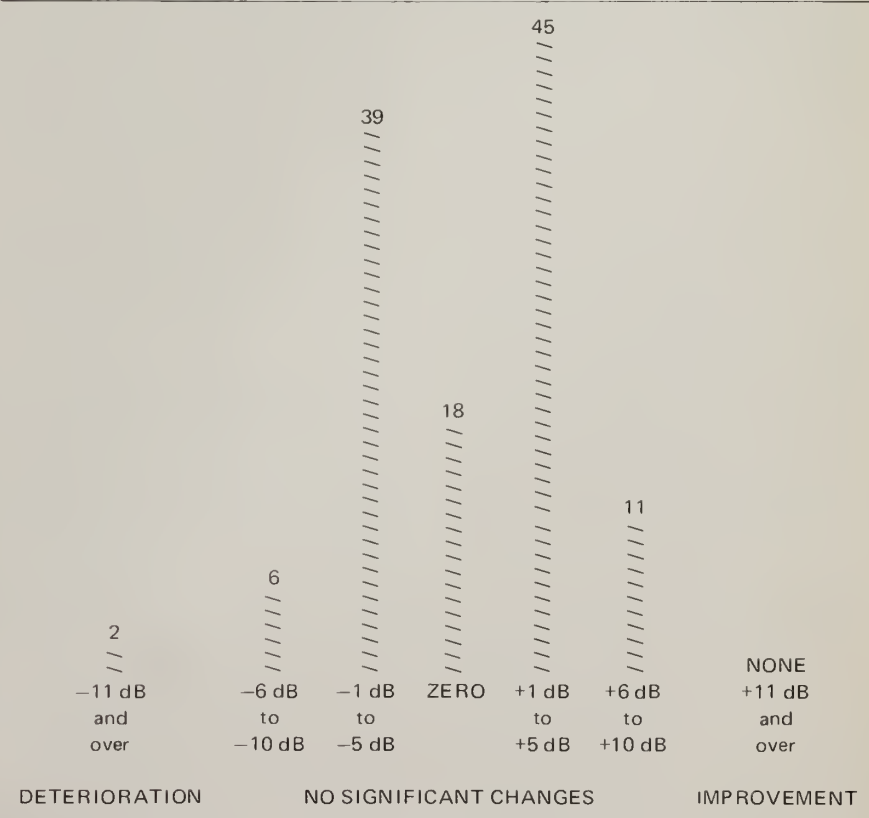
We have chosen to define as "significant" any change in pure tone or speech reception thresholds that exceeds ten decibels. Changes of ten decibels or less are not considered significant since they are commonplace observations during test-retest situations in untreated patients; they are considered to be within the range of error of the testing methods and equipment.⁶ Similarly, the speech discrimination scores must change beyond an arbitrary figure of 10% to be considered significant in this study.⁷

This group of patients included ages from three to 82 years with hearing losses ranging from mild to profound. All had nerve type losses, many were of congenital or hereditary origin, a few were the result of ototoxic drugs, excessive noise, infectious disease, or the aging process.

The number of acupuncture treatments was known in 48 cases. One underwent as few as two treatments; 35 was the largest number. The majority received 5-20 treatments. Differences in age, cause or severity of hearing loss, and number of treatments appeared to make no differences on the effect of acupuncture on hearing.

Table 1 summarizes the changes in the averaged thresholds of the three frequencies of pure tones for every

TABLE 1: Shifts in Averaged Pure Tone Thresholds After Acupuncture in 121 Ears of 64 Patients



ACUPUNCTURE FOR DEAFNESS

FAIRBANKS, WALLENBERG AND WEBB

treated ear in the entire series of patients. No patient experienced more than ten decibels of improvement, but two suffered more than ten decibels of deterioration in one ear.

Table 2 summarizes the changes in speech reception threshold for every treated ear in the entire series of patients. All changes were within ten decibels of the pre-treatment level except for one ear which showed a 14 decibel deterioration. Curiously, this same ear appeared to improve in discrimination while the speech reception deteriorated.

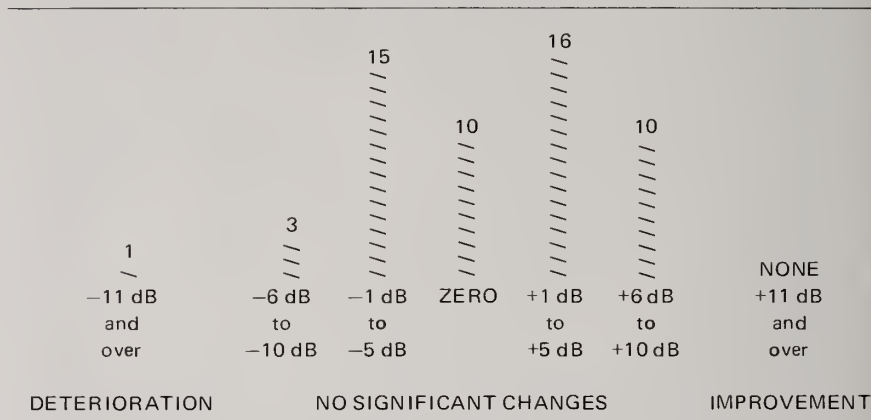
Table 3 summarizes the changes in speech discrimination for each treated ear in the twenty six patients who were tested for this indicator of hearing. Sixteen patients (thirty five ears) showed no significant changes. Three patients (six ears) showed improvement compared to seven patients (eight ears) who suffered deterioration.

Discussion

As a treatment for deafness in the sixty-four patients in this study, acupuncture appears to have had disappointing results. This is even more disheartening when one considers the high cost of such a treatment regimen which requires long distance travel, lodging away from home and time lost from employment. The treatment fees alone could easily exceed the price of a hearing aid and auditory training. Yet the same irrationality that typifies the acupuncture community and pervades its promotional information seems to captivate these patients or parents with desperate hope.

This study describes hearing in one hundred twenty one ears of sixty-four deaf or partially deaf patients that were treated by acupuncturists in the Washington, D.C. centers. Audiograms taken before and after such treatments were analyzed to document any sub-

TABLE 2: Shifts in Speech Reception Thresholds After Acupuncture in 55 Ears of 29 Patients



stantial changes in pure tone thresholds, speech reception thresholds and speech discrimination. The pure tones examined were those considered most representative of hearing in the speech ranges since it is human communication that affords social adjustment and economic well being. Not a single patient exceeded the ten decibels of change which could be considered as a significant improvement. Speech reception thresholds were similarly unaffected.

Speech discrimination scores showed the greatest variability in this study. One wishes for a control group with similar hearing loss levels for comparative purposes, since severely impaired patients often show wider variability than the mildly impaired in test-retests of this indicator. Frequently tested patients do become familiar with the word lists. Consequently their discrimination scores may improve. Yet the number of patients in this study who did score higher in discrimination was offset by a larger number who exhibited deterioration.

Deterioration of hearing after treatment is a thought that apparently has not occurred to the acupuncturists. If it is more than a testing artifact, the authors would ascribe it to unrelenting progression of the disease rather than to any effect of the acupuncture needles.

This study was restricted to the measurable indicators of hearing and we did not attempt to evaluate any subjective changes that patients may have claimed. Subjective (non-measurable) improvements account for many of the testimonials that have reached the popular press. We anticipate that subsequent reports will assess this factor.

This study suggests that acupuncture is a most questionable remedy for deafness. Physicians should be candid with their hearing impaired patients about the futility of such treatments. The authors concede that a certain number of patients—or more particularly, parents of deaf patients—will feel compelled to “leave no stone unturned” even in the face of data such as that presented. They should be

TABLE 3: Changes in Speech Discrimination Scores After Acupuncture in 49 Ears of 26 Patients

2	2	2	2	9	5	6	7	8	2	1	3	NONE
-30%	-24%	-18%	-12%	-6%	-2%	ZERO	+2%	+6%	+12%	+18%	+24%	+30%
and	to	to	to	to	to		to	to	to	to	to	and
over	-28%	-22%	-16%	-10%	-4%		+4%	+10%	+16%	+22%	+28%	over
DETERIORATION				NO SIGNIFICANT CHANGES				IMPROVEMENT				

made aware that at the present time acupuncture is uncontrolled human experimentation.

Acknowledgment

Anne E. Caldwell, M.D., National Library of Medicine, conducted a literature search of the 2300 journals covered by INDEX MEDICUS.

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Smith, MA, Division of Speech and Hearing, Prince George's County Health Department, DC; Robert E. Pumphrey, MD, Ear, Nose, and Throat Medical Group of Washington, DC; David M. Resnick, PhD, Hearing and Speech Center, Washington Hospital Center, Washington, DC; Connie Serota, MA, University of Maryland Hearing and Speech Center, College Park, Md; Hiroshi Shimizu, MD, Johns Hopkins Hospital Hearing and Speech Center, Baltimore; Allen Cheverly, Md; Beth Urban, PhD, Hearing, Language, and Speech Service, Montgomery County Department of Health, Rockville, Md; Ellis A. Wallenberg, MS, Washington Hearing and Speech Society, Washington, DC; Alvin P. Wenger, MD, Greater Baltimore Medical Center, Baltimore; Eleanor S. Wintecorn, PhD, Audiology and Speech Pathology Service, Veterans Administration Hospital, Washington, DC.

References

1. SAWISLAK, A. B.: Acupuncture Holds New Hope for Nerve Deaf, *The Daily News Journal* (Murfreesboro, Tenn.), Sept. 12, 1973, p. 24.
2. KOH, E. K.: Acupuncture, *The Journal of The Royal College of General Practitioners*, Apr. 1973, 23:265-272.

3. PENG, A.: Acupuncture Treatment for Deafness, A Preliminary Report, *American Journal of Chinese Medicine*, 1973, 1:155-158.
4. KAO, F. F., BAKER, R. H., LEUNG, S. J., SLIPPEN, M., AMPOLSAKDI, T., LAPIDOT, A.: Efficacy of Acupuncture for the Treatment of Sensorineural Deafness, *American Journal of Chinese Medicine*, 1973, 1:283-304.
5. KAO, F. F. (translator): Acupuncture Therapeutics for Deaf-mutism, *American Journal of Chinese Medicine*, 1973, 1:361-364.
6. GARNER, W. R.: Auditory Thresholds of Short Tones as a Function of Repetition Rates, *Journal of the Acoustical Society of America*, 1947, 19:600-608.
7. DAVIS, H., SILVERMAN, S. R. (Editors): *Hearing and Deafness*, Third Edition, New York, Holt, Rinehart and Winston, Inc., 1970, p. 214.

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Reprint requests may be addressed to Dr. Fairbanks at Ear, Nose and Throat Medical Group of Washington, 2141 K St., N.W., Washington, D.C. 20037.

For an organization supposedly opposed to change, the AMA has made a lot of changes.

One of the most significant was the addition of an important new voice in the AMA—that of interns and residents. For the first time, these young physicians have not only a voice but also a vote in helping shape AMA policies.

Recently, the AMA House provided the same opportunities for membership and participation to medical students.

That's not all. In another important change, the AMA's council-committee structure has been streamlined. Some councils and committees have been dropped. Others have been made more efficient by reducing their size to seven members for councils and five for committees. And to permit more frequent infusion of new

members and ideas, maximum tenure of service has been reduced to seven and five years, respectively.

The AMA *has* made a lot of changes. Changes to make it more responsive to the ideas of *all* physicians... changes to make it more effectively serve the needs of the profession.

Change will continue. But it will be decided only by those of you interested and dedicated enough to be a force in that change.

**Join us.
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INDICATIONS: *Therapeutically*, used as an adjunct to appropriate systemic therapy for topical infections, primary or secondary, due to susceptible organisms, as in:

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- secondarily infected dermatoses (eczema, herpes, and seborrheic dermatitis)
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Prophylactically, the ointment may be used to prevent bacterial contamination in burns, skin grafts, incisions, and other clean lesions. For abrasions, minor cuts and wounds accidentally incurred, its use may prevent the development of infection and permit wound healing.

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PRECAUTION: As with other antibiotic preparations, prolonged use may result in overgrowth of nonsusceptible organisms and/or fungi. Appropriate measures should be taken if this occurs. Articles in the current medical literature indicate an increase in the prevalence of persons allergic to neomycin. The possibility of such a reaction should be borne in mind.

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The Antacid Analogy



Indications: Pro-Banthine is effective as adjunctive therapy in the treatment of peptic ulcer. Dosage must be adjusted to the individual.

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Warnings: Patients with severe cardiac disease should be given this medication with caution.

Fever and possibly heat stroke may occur due to anhidrosis.

In theory a curare-like action may occur, with loss of voluntary muscle

control. For such patients prompt and continuing artificial respiration should be applied until the drug effect has been exhausted.

Diarrhea in an ileostomy patient may indicate obstruction, and the possibility should be considered before administering Pro-Banthine.

Precautions: Since varying degrees of urinary hesitancy may be evidence by elderly males with prostatic hypertrophy, such patients should be advised to micturate at the time of taking the medication.

Overdosage should be avoided in patients severely ill with ulcerative colitis.

Adverse Reactions: Varying degrees of drying of salivary secretions may

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Antacids have only one mode of action to relieve ulcer pain...

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Antacids:

Antacids relieve ulcer pain by neutralizing gastric acid. This action is relatively short-lived and they have no other mode of action.

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Pro-Banthine suppresses gastric acid secretion. The antisecretory properties of Pro-Banthine are well established. By effectively blocking vagotonic impulses Pro-Banthine suppresses gastric secretion to reduce both total and free acid.

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Pro-Banthine reduces acidity without subsequent acid rebound. The capacity of Pro-Banthine to reduce the secretion of total and free acid in the stomach has been demonstrated in scores of studies. None has demonstrated any significant evidence of acid rebound.

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*Innes, I.R., and Nickerson, M., in Goodman, L.S., and Gilman, A. (editors): The Pharmacological Basis of Therapeutics, ed. 4, New York, The Macmillan Company, 1970, p. 537.

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occur as well as mydriasis and blurred vision. In addition the following adverse reactions have been reported: nervousness, drowsiness, dizziness, insomnia, headache, loss of the sense of taste, nausea, vomiting, constipation, impotence and allergic dermatitis.

Dosage and Administration: The recommended daily dosage for adult oral therapy is one 15-mg. tablet with meals and two at bedtime. Subsequent adjustment to the patient's requirements and tolerance must be made.

Pro-Banthine P.A.—Each tablet of Pro-Banthine P.A. (propantheline bromide) contains 30 mg. of the drug in the form of sustained-release or

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How Supplied: Pro-Banthine is supplied as tablets of 15 and 7.5 mg., as prolonged-acting tablets of 30 mg. and, for parenteral use, as serum-type vials of 30 mg.

Before prescribing, see complete prescribing information in SK&F literature or PDR. The following is a brief summary.

Indications: Edema associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. Also, mild to moderate hypertension.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (> 5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities.

Accordingly, check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently — both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triarterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides.

Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk.

This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Anti-hypertensive effects may be enhanced in post-sympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting may indicate electrolyte imbalance, diarrhea, constipation, other gastrointestinal disturbances. Rarely, necrotizing vasculitis, paresthesias, icterus, pancreatitis, and xanthopsia have occurred with thiazides alone.

Supplied: Bottles and Single Unit Packages of 100 capsules.

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Serum Potassium Level Drops During Long-Term Exercise, *Medical Tribune*, July 4, 1973.

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Is there a need for a drug compendium?

A drug compendium of the type I envision would fill a definite need for the practicing physician. Such a compendium would give him all the information necessary for using a drug intelligently, and it would do so in a clear, concise, convenient, objective and balanced fashion.

What a Compendium Should Contain

I believe the compendium should inform the doctor what a drug will do, when he should use for what type of patient, for how long, in what dose, what benefits his patient is likely to obtain, the risks involved, and cross-reaction with other drugs.

The information would be based on the package insert and have the same legal status. In fact a complete compendium with complete and current information might even eliminate the necessity

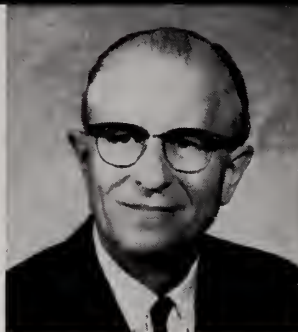
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A drug compendium, or preferably compendia, should, I believe, be private, not federal, in sponsorship. They should contain comprehensive listings of drugs available for prescribing. They should be single, legibly printed volumes of reasonable size, updated quarterly or semiannually and completely revised every year.

Function of a Compendium

A compendium should furnish the following information on drugs in the following order: indications for use, side effects, adverse drug reactions, contraindications, drug interactions, drug dosage at the dosage forms marketed. Drug prices should not be included because they vary so widely and change rapidly.

No compendium should set forth drugs of choice or discuss relative efficacy. Such questions must be left for the practicing physician to decide, whether on the basis of the medical literature, his own clinical experience, advice of colleagues, information supplied by manufacturers, and so on.

Nor should a compendium undertake to educate the doctor on how to use drugs. Rather, it must be a reference source designed primarily to refresh his memory as to drugs he may not use regularly. It

Opinion & Dialogue

for a package insert in many instances. This would constitute a substantial saving for the manufacturer.

By a complete compendium, I do not mean a volume of prohibitive size. You don't need a book describing 25,000 products with an enormous amount of repetition. If, rather, drugs should be arranged by class. Mutually applicable information would be provided, along with brief discussions pinpointing differences in specific drugs of each class. Listings would be cross-indexed in a useful way.

Other Available Documents as Sources of Information

Existing references such as the PDR and the AMA Drug Evaluation are obviously useful but they are incomplete. Either they are not cross-referenced by generic name or they do not group drugs with similar characteristics, or they do not include all the available and legally marketed drugs. And some of those omitted may be very useful.

should in no way imply control over a practitioner's prerogatives.

Why Another Compendium?

A practicable, single-volume compendium cannot, nor is it necessary to, include all drugs on the market today. From my practice of internal medicine for some 30 years, my experience as a consultant, and as a faculty member at four or five medical schools, I would estimate that a doctor uses only 30 to 35 drugs regularly. The 1972 Physicians' Desk Reference, incidentally, contained about 500 entries.

As to whether there should be a federal compendium, in my opinion, as stated earlier, the answer is easy—there should *not* be one. The proposal assumes that existing compendia are inadequate. We're not sure of that at all. Whatever its imperfections, the present drug information system in the U.S. is open, multifaceted, pluralistic and extensive. Good compendia exist, as well as other ample sources on drug therapy, ranging from journal literature through AMA Drug Evaluation to company materials. Not all physicians may use such sources as often or as well as they should, but that is the fault of the user, not of the sources.

In any event, rather than pro-

On the other hand, drugs made by more than one supplier, tetracycline for example, may be fully described a dozen times in the same book.

While perhaps PDR could be rearranged and cross-indexed with generics included, and while the AMA Drug Evaluation might also be modified and expanded, I am not sure that the end result would have all the attributes required for a useful compendium. At the same time, you would run the risk of amassing a voluminous and unwieldy tome.

Should Editorial Comments Accompany the Listings?

Subjective judgments, in my opinion, have no place in a compendium. However, if there is substantial evidence based on a sound body of science concerning relative efficacy of several drugs, certainly that information should be included. The committee of experts compiling and editing a particular section would also have to assess

duce another book, it makes much more sense to work on improving existing compendia, and perhaps they could, as knowledge advances, include more accumulated clinical data and experience, and more information on drug interactions and adverse reactions.

Implications of a Federal Compendium

Take a hard look at the implications of a federal compendium. It would have the force of law, virtually dictating what drugs to use and how to use them. In effect, it would be a regulatory document with legal or quasi-legal status, posing medical/legal problems similar to those the doctor may now encounter if and when he departs from the provisions of the package insert. A compendium under federal aegis would tend to restrict decisions on drug therapy to one orthodox level—a most dangerous trend for medicine.

New Compendium—A Medical Option

I detect no ground swell of initiative or support whatsoever for a federal compendium—or, for that matter, for a new compendium of any type. A 1969 PMA survey conducted by Opinion Research Corporation found that only 15 per

and indicate instances where a meaningful difference between drugs is pertinent.

Sponsorship, Compilation and Editing

Producing a book like this would undoubtedly be difficult and demanding. It would obviously take a great deal of talent and expertise, and would require a varied and experienced group, ranging from writers and editors to highly skilled clinicians and pharmacologists. Style, format and clarity of language would play an important part in determining the usefulness of the book. And it should be updated periodically and completely revised annually.

I have no opinion whether the government or the private sector should sponsor and/or finance the compendium. What is most important is that the compendium be an authoritative, objective and useful source of information for the doctor to have at hand as a ready reference.

cent of those physicians interviewed felt a new compendium was needed. And a large majority did not favor the involvement of the federal government if one were to be created, preferring instead a nongovernmental consortium.

Even if we come to a time when the medical profession itself opts for a new kind of compendium, it should be handled and financed, ideally, outside both government and industry. Final review and editorial authority could be delegated, say, to specialty bodies and medical societies—but above all, *not* the government.

Surely the health care system in the United States has far more vital matters to consider than the extensive cost and effort that would have to go into the preparation and maintenance of a new, monolithic compendium, and especially one bearing the imprimatur of the federal government.

Opinion & Dialogue

What is your opinion, doctor? We would welcome your comments.

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What does man have in common with Samson?

Neither man nor the gorilla can synthesize vitamin C. Interestingly, the slow loris, a primate much further down the evolutionary scale, can convert L-1,4-gulonolactone to ascorbic acid in its liver and presumably does not require an exogenous source of ascorbic acid.

Because man can neither synthesize vitamin C nor store most of the water soluble vitamins, these nutrients must be replenished continuously in order to

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Generally, this is accomplished in his daily diet. But under conditions of illness, stress, in convalescence or following surgery, vitamin stores may be depleted or metabolic demands increased.

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BOOK REVIEWS

Gastrointestinal Pathology by BASIL C. MORSON AND I.M.P. DAWSON with a forward by SIR FRANCIS AVERY JONES. Price \$42.00. Pp 676. Oxford, Blackwell Scientific Publications., 1972.

Morson and Dawson present a well considered review of gastrointestinal pathology designed as much for the clinician as for the pathologist. One of their expressed aims is to facilitate communication between the clinician and the pathologist so essential to optimal patient care. In this they have largely succeeded. Although there is an extensive bibliography the authors have depended primarily on their own experience in arriving at conclusions and opinions. Wisely, they have limited themselves to a discussion of the gastrointestinal tract proper, and have omitted any consideration of the liver, gallbladder or pancreas.

The book is well organized and very well illustrated. A major weakness of the book is the scant attention paid to knowledge gained by the use of the electron microscope.

In reading the book, the reviewer was impressed by the lucidity with which a number of subjects was discussed, e.g. the differentiation between argentaffin cells (associated with the carcinoid syndrome and the elaboration of five-hydroxy tryptamine) and argyrophil cells (believed to secrete gastin and glucagon). The discussion of regional enteritis and vascular diseases of the small intestine was particularly good. The pathologist's special role in handling and interpreting small intestinal biopsies is well presented and here again should help bridge the gap between gastroenterologist and pathologist.

Pathologic criteria, with the differentiation of chronic ulcerative colitis and Crohn's disease, are clearly outlined. The importance of rectal biopsy in distinguishing ulcerative colitis from Crohn's disease of the colon is emphasized. The authors advocate periodic rectal biopsy in patients with long standing ulcerative colitis in an effort to detect a pre-cancerous state and thereby select those patients who should be considered for a proctocolectomy for cancer prophylaxis or treatment. Microscopic features of this pre-cancerous state are carefully presented.

The authors have done us all a service in their treatment of the colonic poly-cancer question. They have divided benign polyps into those which are neoplastic and therefore potentially pre-malignant and those which are not neoplastic and therefore have no malignant potential. Their description of the gross appearance would enable the endoscopist or surgeon to make this distinction at once in most cases.

The book is handsomely printed and illustrations are clear and well chosen. It would make a useful addition to the library of the student of gastroenterology.

THOMAS S. SAPPINGTON, M.D.

Manual of Cardiac Arrhythmias. MICHAEL BILITCH, M.D. Price, \$12.50. Pp. 320. Boston, Massachusetts: Little, Brown & Company, 1971.

Dr. Bilitch emphasizes in his preface that his is "a practical book dealing with the techniques of arrhythmia detection and treatment," and reflects his years of experience and known dedication in the educational process of medical students and house officers. As any book of this type, it has a tendency to over-emphasize the author's areas of special interest at the expense of completeness. Thus, the techniques for insertion of temporary pacemakers and other non-pharmacological means of therapy occupy a lengthy section of the book although they are not discussed in great depth. Contrariwise, new techniques for electrophysiological investigation and diagnosis, i.e., his bundle electrocardiography are not covered and hence concepts such as concealed conduction, re-entry and the differential diagnosis between ventricular tachycardia and supraventricular tachycardia with aberrant conduction is presented without the benefits of up-to-date knowledge and new documentation of electrophysiological concepts.

The chapter on anti-arrhythmic drugs covers well the rules of administration and dosages and presents a logical approach to the pharmacological handling of arrhythmias. Similarly, the various rhythm disturbances are presented in a well-organized manner and the electrocardiographic criteria for their recognition are explicitly outlined, easily understood and without great depth in the differential diagnosis.

The book is nicely presented, the examples well selected and the electrocardiograms and the accompanying ladder diagrams are easy to follow. There is a slight abuse on simplistic drawings and diagrams on techniques and methods for diagnosis and treatment that fail to serve defined purpose.

It is difficult to define a precise audience for texts of this type. The nature of the presentation excludes the basic student who lacks any prior knowledge of electrocardiography and arrhythmias and makes it too superficial for the

cardiologist-electrocardiographer or electrophysiologist. The text, however, should be helpful to those for whom it was primarily directed, namely, house officers and medical students. It will also be helpful to the nurse clinicians and Coronary Care Unit health care personnel needing a basic understanding of the rhythm disturbances covered in this text. For this large and ever-growing group, Dr. Bilitch's approach appears concise, clear, objective and well presented and will serve as an operational manual for the day to day handling of emergency room and coronary care unit problems.
JORGE C. RIOS-PRADIER, M.D.

The Use of X-ray Techniques in Forensic Investigations. DANIEL GRAHAM, F.S.R. Price, \$13.50. Pp. 142. Baltimore, Maryland: The Williams & Wilkins Company, 1973.

This is an excellent monograph on the use of radiology in forensic medicine. The author is a British pathologist, who has apparently done considerable forensic investigation for police authorities. The presentation is primarily technical in nature, and considerable stress on identification by X-ray methods, for use in court, is noted throughout the book.

A chapter on document examination, using an electrostatic process in combination with the X-ray beam, is of interest, as well as the use of Grenz rays for similar purposes.

The text is of interest primarily to those dealing with the highly specialized field of forensic medicine, but, like many specialized monographs, it may contain some knowledge of vital importance at a given moment. It is recommended for the library of those interested in forensic medicine or pathology.
GEORGE TIEVSKY, M.S.

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Ralph W. Lee & Company 6
Mutual of Omaha 4

Nurse Registries

District of Columbia Manpower
Administration T-388

Nutrition Education

Dairy Council of Greater Metropolitan
Washington, D.C. 2

Pharmaceuticals

Abbot Laboratories T-380
Burroughs Wellcome & Company T-373
Dorsey Laboratories 9
Flint Laboratories T-377
Eli Lilly & Company 12
Pharmaceutical Manufacturers
Association T-378
Roche Laboratories C2, 1, C3, C4
G. D. Searle & Company
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Peoples Drug Stores T-383

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For further information on this subject, the following references are provided:

1. Henry BW, et al: *Dis Nerv Syst* 30:675-679, Oct 1969.
2. Hollister LE, et al: *Arch Gen Psychiatry* 24:273-278, Mar 1971.
3. Claghorn J: *Psychosomatics* 11:438-441, Sept-Oct 1970.



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CONTENTS

SCIENTIFIC ARTICLES

Complications of External Cardiac Resuscitation: A retrospective review and survey of the literature. Robert H. Patterson, M.D., Willard A. Burns, M.D. and Frank S. Jannotta, M.D.	389
Diagnosis and Treatment of Hemodynamic Abnormalities After Acute Myocardial Infarction. H. Joel Gorfinkel, M.D., Riaz Haider, M.D. and Joseph Lindsay, Jr., M.D.	395
A Case Report of Serratia Endocarditis with Review of the Literature. Habib O. Farhoudi, M.D., Tazewell Banks, M.D. and Nayab Ali, M.D.	401
Hypertensive Cerebellar Hemorrhage. William H. Lawrence, M.D.	409
Uhl's Anomaly of the Heart with Atrial Septal Defect and Valvular Pulmonary Stenosis. Robert Obma, M.D., Lowell W. Perry, M.D. and Lewis P. Scott, M.D.	413

SPECIAL ARTICLE

Causes of Death Soon After Injury. William W. Funderburk, M.D.	407
---	-----

OTHER FEATURES

Editorial	5
National Exercise and Heart Disease Project. John Naughton, M.D., Jack Taylor, M.D., Patrick Gorman, M.D. and Jorge Rios M.D.	
Scientific Editorial	9
Intermittent IPPB Treatments: Therapy in Search of an Indication. Philip Witorsch, M.D.	
Post Graduate Education	429
When to Consider Coronary Artery Bypass Surgery. Gerald I. Shugoll, M.D.	
The View Box	411
Edited by Gunter J. Augustin, M.D.	
ECG Problems	412
Edited by Robert R. Montgomery, M.D.	
Information for Authors	433
Advertising and Subscription Information	436
Index to Advertisers	436

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Editorial

NATIONAL EXERCISE AND HEART DISEASE PROJECT

JOHN NAUGHTON, M.D.
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JORGE RIOS, M.D.,
ASSOCIATE PROFESSOR OF MEDICINE

Prospective epidemiological studies such as the Framingham Study have shown that the risk of death from ischemic heart disease rises as living habits become sedentary. Similar findings have come from investigations of occupational physical activity in relation to IHD such as the London bus drivers¹ and the San Francisco longshoreman.² There has not been any adequately controlled study of the long term effect of the intervention of exercise in the life history of ischemic heart disease.

The National Exercise and Heart Disease Project is designed to determine the effects of regular physical activity on the rehabilitation of survivors of myocardial infarction. This national collaborative study has three primary objectives: 1) to determine the influence of regular, individually prescribed, supervised physical activity on the morbidity and mortality of patients with coronary heart disease; 2) to determine the effects of regular physical activity on the patient's psychosocial adjustment following myocardial infarction; and 3) to identify those factors which characterize coronary patients most likely to benefit from a long-term physical activity program.

Following two years' preparation, the study began accepting subjects in the Spring. Eligible subjects are men between the ages of 30 and 64 who have had a documented myocardial infarction within the previous twelve months, who are able to exercise safely at a work load of at least two miles per hour at a 3.5% grade on a treadmill and who have no other diseases which contraindicate exercise such as uncontrolled hypertension or insulin dependent diabetes. Each volunteer must be recommended to

the study by his physician and each patient remains in the care of his physician. The exercise training program is supervised by physicians from the study center. The referring physician will receive those project results which are important in the management of his patient. Subjects referred for study will be screened for eligibility during an initial evaluation, which includes a comprehensive medical history and physical examination, behavioral questionnaire, chest x-ray, resting electrocardiogram, pulmonary function studies, and an exercise stress test. Following the initial evaluation, all eligible volunteers will enter a six-week program of thrice-weekly supervised and monitored low level exercise sessions designed to familiarize participants with the exercise routines and to detect potential "drop outs". Following the preparatory program, all eligible volunteers will be randomly assigned to either an exercise group or a non-exercise group. The exercise group will continue in a thrice-weekly program of supervised and monitored exercise sessions designed to obtain a significant aerobic training effect. The control group will maintain their routine physical activities but will be asked not to enter into any formalized exercise program. Both groups will be evaluated at quarterly intervals throughout the study to detect changes in cardiopulmonary and psychosocial status.

The intensity of exercise performed by each subject will be individually determined and prescribed by a study center physician. All exercises will be undertaken in a supervised setting which provides continuous electrocardiographic monitoring for each individual, and supervision by a team of physician,

physical educators, and physical therapists thoroughly trained in exercise physiology and cardiopulmonary resuscitation. Each study center is equipped to provide immediate cardiopulmonary resuscitation should it ever be necessary.

Four university medical centers will participate in the study under a common protocol. The George Washington University Medical Center will serve as the Coordinating Center for the four centers under the directorship of Dr. John Naughton. The Coordinating Center staff includes Dr. Jack Taylor, Dr. Jorge Rios, Dr. Jerome Cornfield, Mr. Larry Shaw, Mrs. Sarah Schesselman, and Mrs. Theresa West. Its functions include storage and analysis of all data through the Electrocardiographic Center and the Biostatistics Center. Periodic progress reports of the study together with appropriate summarization of the results will be reported to each medical community through such channels as the Medical Annals of D.C.

Those physicians who desire more information about the study or to refer patients to the study should contact the center director in his area.

The Collaborating Centers and their directors are: The University of Alabama, Dr. Albert Oberman; Case-Western Reserve University, Dr. Herman Hellerstein; Emory University, Dr. Charles Gilbert; and the George Washington University Medical Center, Dr. Patrick Gorman.

References

1. Morris, J. N., Heady, J. A., Raffle, P. A. B., Roberts, C. G., and Parks, J. W.: "Coronary Heart Disease and Physical Activity of Work". *Lancet* 2:1053-1111, 1953.
2. Paffenbarger, R. S., Laughlin, M. E., Giwer, A. S., and Black, R. A.: "Work Activity of Longshoremen as Related to Death from Coronary Heart Disease and Stroke". *NEJM* 282:1109, 1970.

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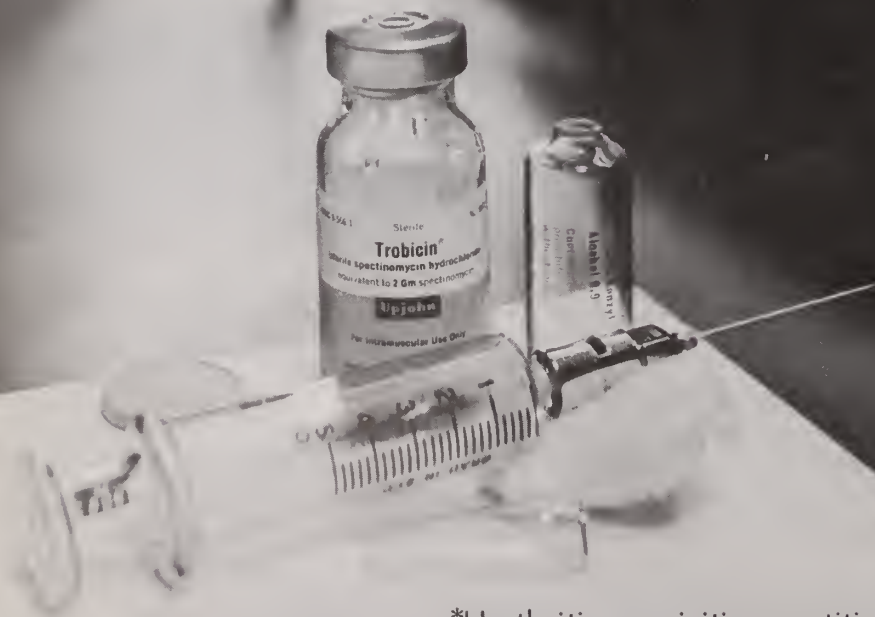
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Contraindications: Contraindicated in patients previously found hypersensitive to spectinomycin.

Warnings: Not indicated for the treatment of syphilis. Antibiotics used to treat gonorrhea may mask or delay the symptoms of incubating syphilis. Patients should be carefully examined and monthly serological follow-up for at least 3 months should be instituted if the diagnosis of

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[†]For patients with gonorrheal proctitis and for patients in geographic areas where antibiotic resistance is known to be prevalent, initial treatment with 4 grams is preferred.

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SCIENTIFIC Editorial

Intermittent IPPB Treatments: Therapy in Search of an Indication.

PHILIP WITORSCH, M.D.

Although intermittent positive pressure breathing (IPPB) for the treatment of lung disease was first introduced over a quarter of a century ago¹, it remains a most controversial and confusing area of medicine. Since that time, techniques involving IPPB have been applied in a variety of dissimilar situations, ranging from treatments of 10 to 20 minutes duration several times a day administered via a mouthpiece or mask at home to continuous assisted or controlled mechanical ventilation administered via an endotracheal or tracheostomy tube on an intensive care unit in a hospital (2-8). While there are differences of opinion regarding techniques, methods, types of equipment, and specific indications for its institution, there is general agreement that IPPB has a significant role when used as a means of continuous assisted or controlled mechanical ventilation in many patients with acute respiratory failure⁹⁻¹¹. On the other hand, the intermittent use of IPPB as treatments continues to generate considerable controversy^{9,10}.

The use of intermittent IPPB treatments has been advocated as a better method to deliver bronchodilator aerosols to ambulatory patients with chronic obstructive lung diseases and, in fact, such techniques and equipment are widely used at enormous cost for this purpose^{3,5,9}. Unfortunately, there is little, if any, good objective evidence to support the contention that the use of IPPB for this purpose offers any advantages over the use of simpler and less expensive techniques. Carefully done studies comparing the administration of bronchodilator aerosols using IPPB devices versus hand-bulb nebulizers and other non-IPPB methods have revealed that changes in ventilatory measurements immediately after treatment were identical whether bronchodilators were delivered using IPPB or non-IPPB methods^{4,12-14}. Other studies have failed to show any survival benefit or advantage regarding rate of deterioration in pulmonary function when patients with chronic obstructive pulmonary disease who used IPPB treatments as part of their

comprehensive program of therapy were compared with a matched group of patients who did not utilize IPPB treatments in their therapy program¹⁵. Similarly, when such parameters as arterial blood gases, airway resistance, alveolar ventilation, dead-space ventilation, and patient fatigue during and after the treatment have been evaluated in carefully controlled studies, there has been no advantage demonstrated to the delivery of bronchodilator aerosols by IPPB as compared with other methods¹⁶⁻¹⁹.

It has been proposed that IPPB is useful to reduce the work of breathing and to thus relieve the fatigue resulting from the excessive muscular work involved in maintaining ventilation in patients with chronic lung disease⁹. While there is little question that continuous assisted or controlled mechanical ventilation using IPPB, when properly applied, considerably reduces the work of breathing and the fatigue resulting therefrom²⁰, it does not necessarily follow that a similar beneficial effect exists when IPPB is used for intermittent treatments. In fact, carefully done studies show no advantage and sometimes a disadvantage related to the patient improperly using the IPPB machine^{10,17,18,21}.

IPPB treatments administered intermittently have been proposed as an adjunct to the conservative management of acute respiratory failure⁹. Again, there is little or no evidence that the use of IPPB treatments in this manner adds anything to therapy using such modalities as low flow oxygen administration, intensive and meticulous nursing care, intensive attention to airway secretions, aerosol, humidity and bronchodilator therapy administered by non-IPPB techniques, antibiotics, and intensive pulmonary physiotherapy, in the conscious patient with acute respiratory failure. When such patients do not respond to such measures or become so fatigued by the work of breathing that they are unable to maintain adequate ventilation, endotracheal intubation and continuous assisted or controlled mechanical ventilation may become necessary. There

is no evidence that the use of IPPB treatments on an intermittent basis at any stage in the conservative management of acute respiratory failure adds anything to these other measures relative to avoiding the ultimate need for continuous mechanical ventilation.

Another area in which the intermittent use of IPPB treatments has been proposed has been in the post-operative state, as a means of preventing post-operative pulmonary complications^{2,2}. When this has been looked at critically, however, there has been no demonstrable difference in the incidence of post-operative pneumonia or atelectasis when IPPB treatments have been used as compared to regimens in which IPPB was not used^{2,3,24}.

In contrast to the paucity of evidence supporting the efficacy of intermittent IPPB treatments, there is a considerable body of data involving complications and adverse affects of IPPB. These include adverse cardiovascular effects^{2,5}, pneumothorax^{2,8}, respiratory infection^{2,7}, and monetary cost^{10,11,28}, to mention but a few. While it might be said that such adverse affects are more significant with IPPB used for continuous mechanical ventilation than for intermittent treatments and are not limited to the latter, it is also in the latter that evidence sufficient to justify even minimal risk and expense is most unimpressive.

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References

- Motley, H. L., Werko, L., Cournand, A., and Richards, D., Jr.: Observations on the Clinical Uses of Intermittent Positive Pressure. *J. Aviation Med.*, 1947, 18, 417.
- Motley, H. L., Cournand, A., Werko, L., et al.: Intermittent Positive Pressure Breathing: A Means of Administering Artificial Respiration in Man. *JAMA*, 1948, 137, 370.
- Petty, T. L. and Broughton, J. O.: A New, Simple IPPB Device for Hospital and Home Use. *JAMA*, 1968, 203, 871.
- Fowler, W. S., Helmholtz, H. F., Jr., and Miller, R. D.: Treatment of Pulmonary Emphysema with Aerosolized Bronchodilator Drugs and Intermittent Positive-Pressure Breathing. *Mayo Clin. Staff Proc.*, 1953, 28, 743.
- Sheldon, G. P.: Pressure Breathing in Chronic Obstructive Lung Disease. *Medicine*, 1963, 42, 197.
- Jessen, O., Kristensen, H. S., and Rasmussen, K.: Tracheostomy and Artificial Ventilation in Chronic Lung Disease. *Lancet*, 1967, 2, 9.
- Ambraveger, M., Jones, E. S., and Roberts, D. V.: Intermittent Positive Pressure Ventilation in Severe Asthma. *Anaesthesia*, 1967, 22, 134.
- Pierce, A. K.: Assisted Respiration. *Ann. Rev. Med.*, 1969, 20, 431.
- Mayock, R. L.: IPPB is a Useful Modality in the Treatment of Chronic Obstructive Lung Disease. In Ingelfinger, F. J., Ebert, R. V., Finland, M., and Relman, A. S. (eds): *Controversy in Internal Medicine II*. Philadelphia, W. B. Saunders Company, 1974, p. 249.
- Miller, R. D., and Hepper, N. G. G.: The Dangers and Limitations of IPPB in Managing Diseases Affecting Ventilation. In Ingelfinger, F. J., Ebert, R. V., Finland, M., and Relman, A. S. (eds): *Controversy in Internal Medicine II*. Philadelphia, W. B. Saunders Company, 1974, p. 263.
- Ebert, R. V.: The Place of IPPB in the Management of Chronic Obstructive Lung Disease. In Ingelfinger, F. J., Ebert, R. V., Finland, M., and Relman, A. S. (eds): *Controversy in Internal Medicine II*. Philadelphia, W. B. Saunders Company, 1974, p. 272.
- Miller, R. D., Fowler, W. S., and Helmholtz, H. F., Jr.: The Treatment of Pulmonary Emphysema and of Diffuse Pulmonary Fibrosis with Nebulized Bronchodilators and Intermittent Positive Pressure Breathing. *Dis. Chest*, 1935, 28, 309.
- Leslie, A., Dantes, A., and Rosove, L.: Intermittent Positive-Pressure Breathing: Appraisal of Use in Bronchodilator Therapy of Pulmonary Emphysema. *JAMA*, 1956, 160, 1125.
- Goldberg, I. and Cherniak, R. M.: The Effect of Nebulized Bronchodilator Delivered With and Without IPPB on Ventilatory Function in Chronic Obstructive Emphysema. *Amer. Rev. Respir. Dis.*, 1965, 91, 13.
- Curtis, J. K., Liska, A. P., Rasmussen, H. K., et. al.: IPPB Therapy in Chronic Obstructive Pulmonary Disease: An Evaluation of Long-term Home Treatment. *JAMA*, 1968, 206, 1037.
- Lefcoe, N. and Carter, P.: Intermittent Positive-Pressure Breathing in Chronic Obstructive Pulmonary Disease. *Canad. Med. Ass. J.*, 1970, 103, 279.
- Segal, M. S., Salomon, A., Dulfano, M. J., et. al.: Intermittent Positive Pressure Breathing: Its Use in the Inspiratory Phase of Respiration. *New Eng. J. Med.*, 1954, 250, 225.
- Kamat, S., Dulfano, M. J., and Segal, M. S.: The Effect of Intermittent Positive Pressure Breathing (IPPB/II) with Compressed Air in Patients with Severe Chronic Nonspecific Obstructive Pulmonary Disease. *Amer. Rev. Resp. Dis.*, 1962, 86, 360.
- Cohen, A. A. and Hale, F. C.: Comparative Effects of Isoproterenol Aerosols on Airway Resistance in Obstructive Pulmonary Diseases. *Amer. J. Med. Sci.*, 1965, 249, 309.
- Ayres, S. M., Kozam, R. L., and Lukas, D. S.: The Effects of Intermittent Positive Pressure Breathing on

- Intrathoracic Pressure, Pulmonary Mechanics, and the Work of Breathing. *Amer. Rev. Respir. Dis.*, 1963, 87, 370.
21. Jones, R. H., MacNamara, J., and Gaensler, E. A.: The Effects of Intermittent Positive Pressure Breathing in Simulated Pulmonary Obstruction. *Amer. Rev. Respir. Dis.*, 1960, 82, 164.
 22. Noehren, T. H., Lasry, J. E., and Letgers, L. J.: Intermittent Positive Pressure Breathing (IPPB/I) for the Prevention and Management of Post-operative Pulmonary Complications. *Surgery*, 1958, 43, 658.
 23. Sands, J. H., Cypert, C., Armstrong, R., et al.: A Controlled Study Using Routine Intermittent Positive Pressure Breathing in the Post-surgical Patient. *Dis. Chest*, 1961, 40, 128.
 24. Baxter, W. D. and Levine, R. S.: An Evaluation of Intermittent Positive Pressure Breathing in the Prevention of Post-operative Pulmonary Complications. *Arch. Surg.*, 1969, 98, 795.
 25. Cournand, A., Motley, H. L., Richards, D. W., and Werko, L.: Physiological Studies of the Effects of Intermittent Positive Pressure Breathing on Cardiac Output in Man. *Amer. J. Physiol.*, 1948, 152, 162.
 26. Nennhaus, H., et. al.: Alveolar and Pleural Rupture, Hazards of Positive Pressure Respiration. *Arch. Surg.*, 1967, 94, 136.
 27. Pierce, A. K., Edmonson, E. B., McGee, G., et. al.: An Analysis of Factors Predisposing to Gram-negative Bacillary Necrotizing Pneumonia. *Amer. Rev. Respir. Dis.*, 1966, 94, 309.
 28. Corman, R.: Is This Machine Necessary? *NTRDA Bull.*, 1972, 58, 3.



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SCIENTIFIC ARTICLES

Complications of External Cardiac Resuscitation: A retrospective review and survey of the literature

ROBERT H. PATTERSON, M.D., WILLARD A. BURNS, M.D. AND FRANK S. JANNOTTA, M.D.

Abstract

Complications of external cardiac resuscitation including rupture of the thoracic aorta were found in a retrospective review of two necropsy series. Other complications include fractures of ribs and sternum, bone marrow emboli, hemothorax, hemopericardium, pneumothorax, and laceration of abdominal organs and vessels with hemorrhage. A survey of the literature is presented. Aortic rupture, while rare as a complication of resuscitation, in some instances may be amenable to surgical correction and should be recognized as an entity.

Since the development of external cardiac massage in 1960¹ various complications have been reported. Fracture of ribs, sternum^{2,3,4,5,6,7,8,9} and separation or fracture of costochondral joints¹⁰ are the most common adverse results, especially in older people. The incidence of rib or sternal fracture in reported series varies from 16%⁹ to 75%¹¹ and 80%.¹² Pulmonary bone marrow emboli are common^{3,7,10,13} and may be found in the absence of bone fractures.^{14,15} Fat emboli have also been reported^{16,17}. Vegh-Hansen reported an interesting case in which microemboli in cerebellar arteries were composed of epithelial cells, fragments

The two examples of aortic rupture subsequent to external cardiac resuscitation indicate that this is a more common clinical and pathologic entity than formerly recognized.

of alveolae, clumps of bacteria and clear spaces possibly representing fat or air¹⁵. The possible clinical importance is apparent.

Some complications are life threatening or incompatible with survival even if the event leading to cardiac arrest is reversible. These more immediately serious complications include flail chest,¹³ tension pneumothorax,¹⁸ hemopericardium,^{9,13,16,18} hemothorax,^{3,9,18} lacerations of the liver with hemoperitoneum^{4,5,8,16,19} lacerations of the spleen,^{5,7,8,16} tear of the inferior vena cava from the right atria,⁸ and gastric laceration or rupture^{20,21,22}. The gastric lesions are thought to result from external compression of a dilated stomach secondary to improperly applied mouth to mouth resuscitation. Severe cardiac trauma is infrequent¹⁰ but subepicardial hemorrhages are not uncommon⁴. Rupture of the myocar-

dium may occur but is invariably through an area of infarction⁸.

Nelson and Ashley in 1965 reported a case of aortic rupture attributable to external cardiac massage^{2,3}. We briefly reported two similar cases seen recently, one at The George Washington University Medical Center (GW) and the other at the Washington D. C. Veterans Administration Hospital (VA)²⁴. These two additional cases prompted a retrospective study of necropsy protocols for complications of resuscitation.

Methods and Material

One thousand consecutive necropsy protocols were reviewed from each department. The GW series contained 134 infant necropsies which were excluded for the purposes of this study. Each necropsy protocol was reviewed, admitting the incompleteness of retrospective surveys, to identify those patients on whom resuscitation had been attempted. The two cases with aortic rupture were studied in detail. Microscopic sections of aorta from the areas of rupture and sections of thoracic aorta from two age-matched controls were stained with hematoxylin and eosin, periodic acid Schiff, Alcian blue, and elastic van Geison stains.

COMPLICATIONS OF EXTERNAL CARDIAC RESUSCITATION

PATTERSON, BURNS AND JANNOTTA

Results

The results of the survey are tabulated in Tables I, II, and III. The smaller number of patients on whom resuscitation was attempted at the Veterans Administration Hospital is due primarily to the large number of patients with widespread metastatic carcinoma.

TABLE I

Complications of External Cardiac Resuscitation		
	GW	VA
Cases	866	1000
Resuscitation Attempts	235	142
Complications—# of Patients	51	28
% with Complications	22%	20%
Total Complications	74	38
Major Complications	29	13
Major Complications—# of Patients	17	7
% with Major Complications	7%	5%
% with Major Complications (Excluding Rib Fractures as Only Lesion)	4%	5%

Complications of external cardiac resuscitation occurred in 22% (51 of 235) of the GW necropsy series and in 20% (28 of 142) of the VA necropsy series. Rupture of the myocardium following attempted resuscitation through an area of infarction was not considered to be a complication. Complications were considered to be major in 39% (29 of 74) of the cases in the GW series and 34% (13 of 38) in the VA series. In no instance were microscopic bone marrow emboli common and they were not considered to be functionally significant in any of our cases. In several instances more than one complication resulted from the resuscitative effort. Serious complica-

TABLE II

Minor Complications of External Cardiac Resuscitation					
		GW		VA	
Rib Fractures	Total Cases	40 (33*)	17%	6 (5*)	4%
	1-4 Ribs	28	12%	4	3%
	Unspecified	2	1%	2	1%
Separation of Costochondral Junction		2	1%	—	
Fracture of Sternum		5	2%	—	
Fracture of Clavicle		1	0.4%	—	
Bone Marrow Emboli, Lungs		3	1%	16	11%
Bone Marrow Emboli, Myocardium		—		1	1%
Petechiae Ecchymoses of Epicardium		2	1%	2	1%
Ecchymoses of Mediastinum		1	0.4	—	
Subpleural Hemorrhages of Lungs		1	0.4%	—	

* Only Lesion

TABLE III

Major Complications of External Cardiac Resuscitation					
		GW		VA	
Rib Fractures	5 or More Ribs	10	4%	—	
	Rupture of Thoracic Aorta	1	0.4%	1	1%
Hemomediastinum		—		1	1%
Hemothorax		2*	1%	1	1%
Hemopericardium		2	1%	2	1%
Pneumothorax		2	1%	3*	2%
Subcutaneous Emphysema of Chest		—		1	1%
Subcapsular Hematoma of Liver		3	1%	1	1%
Laceration of Liver		2	1%	1	1%
Laceration of Spleen		1	0.4%	—	
Perforation of Right Accessory Renal Vein		1	0.4%	—	
Retroperitoneal Hematoma		3	1%	—	
Hemoperitoneum		2	1%	2	1%

* One Case Bilateral

tions occurred in 17 of 235 patients (7%) in the GW series and seven of 142 patients (5%) in the VA series. Separating eight patients in the GW series with 5 or more rib fractures as the only major complications, nine of 235 patients (4%) had combinations of other complications.

Discussion

The complications of resuscitation in the GW and VA series are similar to those found in previous autopsy series. Kaplan and Knott^{1,3} reported complications in 28% of 100 patients and Shapir⁹ in 31% of 62 patients. Rib fractures occurred in 24% and 13% of the patients in the respective series. Only 4% of the patients in our VA series had rib fractures. Shapir⁹ and Paaske *et al*² in their reviews of several autopsy series found a great variation in the percentage of patients with rib fractures and found a variable but usually low percentage of serious visceral injuries. Shapir⁹ found a 15% incidence of hemopericardium, a 3% incidence of hemopneumothorax, and no patients with liver injury. Barringer *et al*⁵ in their series found 4% of patients with hemopericardium, 9% with hemopneumothorax, and 11% with liver injury. Paaske *et al*² found a lower occurrence of such injuries. Pneumothorax occurred in 3%, hemothorax in 3%, and liver injury in 2% of his patients. Himmelhock *et al*⁶ found one example (2%) of hemopericardium in his series of 52 patients but had no other complications except rib fractures, and bone marrow and fat emboli. Jude *et al*¹⁰ and Fletcher¹⁸ discuss mechanical reasons for the occurrence of some of these complications.

The two cases of aortic rupture subsequent to external cardiac resuscitation are, to our knowledge, only the second and third reported examples^{2,4}. This is of interest because the condi-

tion in some instances may be amenable to surgical correction.

The first patient was a 70 year old black male who had a cardiac arrest after developing chest pain. Defibrilla-

tion and external cardiac massage were not successful. At necropsy there were fractures of eight right ribs, a 1500 ml left hemothorax, and a small 1 cm tear of the anterior portion of the proximal



FIG. 1. Heart and aorta from first case with pointer through area of rupture in the proximal descending aorta.

COMPLICATIONS OF EXTERNAL CARDIAC RESUSCITATION

PATTERSON, BURNS AND JANNOTTA

descending aorta (Figure 1). Large complicated atheromatous plaques were present but there was no aneurysm. Rupture occurred in an area of severe atherosclerosis (Figure 2). The aorta had some fraying of elastic fibers but no cystic medionecrosis. The heart weighed 480 grams and revealed bilateral ventricular hypertrophy and an old infarct of the lateral left ventricle.

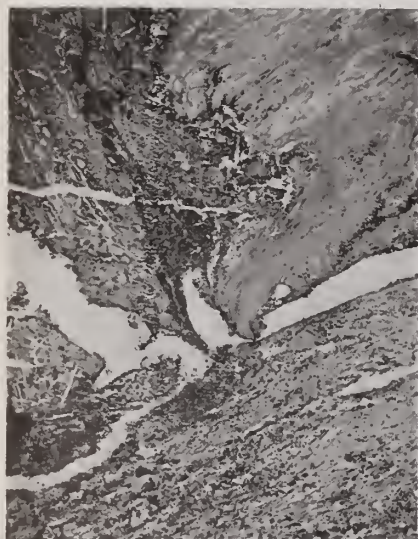


FIG. 2. The lacerated edge of the aorta is present in the upper right hand corner. Atherosclerotic debris is adjacent to the aorta. Hemorrhage extends into the surrounding tissue. Hematoxylin and Eosin X 67.

The second patient was an 80 year old black male with hypertension, atrial fibrillation and congestive heart failure who had a cardiac arrest in the VA Admitting Office. Mechanical external cardiac massage was not successful. Necropsy disclosed increased anterior-posterior diameter and kyphoscoliosis, a 600 to 1000 ml hemopericardium and hemomediastinum, and a small right hemothorax. A ragged tear approximately 2.5 by 2 by 4.8 cm was present in the ascending aorta 6 cm distal to the coronary ostia (Figure 3).

There was minimal atherosclerosis, increase in ground substance and fraying of elastic tissue. The heart weighed 850 grams and had left ventricular hypertrophy. Bone marrow emboli were present in pulmonary vessels, but

there were no rib fractures.

The most frequent cause of aortic rupture is an automobile accident^{2,5}. In a few instances the adventitia of the aorta provides temporary containment or allows for the development of a



FIG. 3. Heart and aorta from second case demonstrating the irregular ragged tear of the ascending aorta. (Reproduced with permission of J.A.M.A.)

chronic aneurysm. If the acute condition is recognized surgical intervention in some cases may be curative^{2,5,6}.

It is not surprising that rupture of a markedly atherosclerotic aorta could occur in conjunction with external cardiac resuscitation. Rodriguez and Rivera^{2,7} in 1961 reported the case of a 58 year old white female with spontaneous rupture of the distal thoracic aorta in an area of marked atherosclerosis but no aneurysm. A similar case resulting in recurrent hemopericardium has also been reported^{2,8}.

The case reported by Nelson and Ashley^{2,3} was that of a 78 year old white female with severe carotid artery atherosclerosis who suffered a cardiac arrest following bilateral carotid arteriograms. The sternum was noted to snap during the unsuccessful resuscitation attempt. At necropsy there was a 300 ml hemopericardium. The ascending aorta was widened and the intima and media were torn circumferentially 3 cm above the aortic arch except for a 2 cm area posteriorly. There were three fractured ribs as well as the fracture of the sternum which overlaid the aortic laceration. The aorta revealed marked atherosclerosis but there was no cystic medionecrosis.

In our first case the aorta revealed large complicated atheromatous plaques while the aorta in the second case revealed only minimal atherosclerosis. In each case the degree of fraying of elastic tissue and mucoid degeneration was not significantly greater than age-matched controls. The fixed, rigid chest of the second patient may have led to overly vigorous resuscitation resulting in extra-ordinary intrathoracic pressure.

The two examples of aortic rupture subsequent to external cardiac resuscitation indicate that this is a more common clinical and pathologic entity than formerly recognized. It is possible that the rupture could occur during

resuscitation of a patient who might be able to withstand surgical repair. Cardiac standstill following an electric shock would be an example. Therefore, it is important to consider this in the differential diagnoses of complications which may occur in a patient who survives resuscitation.

References

1. KOUWENHOVEN, W. B., JUDE, J. R., KNICKERBOCKER, G. G.: Closed-chest cardiac massage. *J.A.M.A.* 1960, 173, 1064.
2. PAASKE, F., HART HANSEN, J. P., KOUDAHL, G., OLSEN, J.: Complications of closed-chest cardiac massage in a forensic autopsy material. *Dan. Med. Bull.* 1968, 15, 225.
3. BARINGER, J. R., SALZMAN, E. W., JONES, W. A., FRIEDLICH, A. L.: External cardiac massage. *New Engl. J. Med.* 1961, 265, 62.
4. BYNUM, W. R., CONNELL, R. M., HAWK, W. A.: Causes of death after external cardiac massage: Analysis of observations on 50 consecutive autopsies. *Cleveland Clin. Quart.* 1963, 30, 147.
5. CLARK, D. T.: Complications following closed-chest cardiac massage. *J.A.M.A.* 1962, 181, 337.
6. HIMMELHOCH, S. R., DEKKER, A., GAZZANIGA, A. B., LIKE, A. A.: Closed-chest cardiac resuscitation. *New Engl. J. Med.* 1964, 270, 118.
7. MINUCK, M.: Organization and experiences of a cardiac resuscitation service. *Can. Anaesth. Soc. J.* 1966, 13, 52.
8. Discussion on complications of cardiopulmonary resuscitation. *Acta. Anaesthesiol. Scand.* 1968, 12, Supplements 29-32, 319.
9. SAPHIR, R.: External cardiac massage: Prospective analysis of 123 cases and review of the literature. *Medicine* 1968, 47, 73.
10. JUDE, J. R., KOUWENHOVEN, W. B., KNICKERBOCKER, G. G.: External cardiac resuscitation. *Monogr. Surg. Sci.* 1964, 1, 59.
11. HENRIKSEN, H.: Rib fractures following external cardiac massage. *Acta. Anaesthesiol. Scand.* 1967, 11, 57.
12. JENSEN, J. B., PEDERSEN, J. L., ROJEL, J.: Elektrisk og medikamentel defibrillation ved ventrikelflimren. *Ugeskr. Laeg.* 1964, 126, 505.
13. KAPLAN, B. M., KNOTT, A. P.: Closed-chest cardiac massage for circulatory arrest. *Arch. Intern. Med.* 1964, 114, 5.
14. SILVERBERG, B., RACHMANOFF, N.: Complications following external cardiac massage. *Surg. Gynecol. Obstet.* 1964, 119, 6.
15. VAGN-HANSEN, P. L.: Complications following external cardiac massage with special emphasis on cerebral embolism. *Acta. Pathol. Microbiol. Scand. (A)* 1971, 79, 505.
16. KLASSEN, G. A., BROADHURST, C., PERETZ, D. I., JOHNSON, A. L.: Cardiac resuscitation in 126 medical patients. *Lancet.* 1963, 1, 1290.
17. LAWRENCE, R. M., HALEY, E. M., GILLIES, A. J.: Closed chest cardiopulmonary resuscitation. *New York State J. Med.* 1964, 64, 2523.
18. FLETCHER, G. F.: Hazardous complications of "closed chest" cardiopulmonary resuscitation. *Amer. Heart J.* 1969, 77, 431.
19. THALER, M. M., KRAUSE, V. W.: Serious trauma in children after external cardiac massage. *New Engl. J. Med.* 1962, 267, 500.
20. DEMOS, M. J., POTICHA, S. M.: Gastric rupture occurring during external cardiac resuscitation. *Surgery* 1964, 55, 364.
21. LUNDBERG, G. D., DAVIS, C. J.: Hemorrhage from gastroesophageal lacerations following closed chest cardiac massage. *J.A.M.A.* 1967, 202, 195.
22. ANTHONY P. P., TATTERSFIELD, A. E.: Gastric mucosal lacerations after cardiac resuscitation. *British Heart J.* 1969, 31, 72.
23. NELSON, D. A., ASHLEY, P. F.: Rupture of the aorta during closed-chest cardiac massage. *J.A.M.A.* 1965, 193, 681.
24. PATTERSON, R. H., BURNS, W. A., JANNOTTA, F. S.: Rupture of the thoracic aorta: Complication of resuscitation. *J.A.M.A.* 1973, 226, 197.
25. RITTENHOUSE, E. A., DILLARD, D. H., WINTERSCHIED, L. C., MERENDINO, K. A.: Traumatic rupture of the thoracic aorta: A review of the literature and a report of 5 cases with attention to special problems in early surgical management. *Ann. Surg.* 1969, 170, 87.

COMPLICATIONS OF EXTERNAL CARDIAC RESUSCITATION

PATTERSON, BURNS AND JANNOTTA

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26. SHEK, J. L.: Nonpenetrating traumatic rupture of thoracic aorta. *Vasc. Surg.* 1971, 5, 211.
 27. RODRIQUEZ, H. F., RIVERA, E.: Spontaneous rupture of the thoracic aorta through an atheromatous plaque. *Ann. Intern. Med.* 1961, 54, 307.
 28. CASTLEMAN, B., MCNEELY, B. U.: Case records of the Massachusetts General Hospital #43, 1970. *New Engl. J. Med.* 1970, 283, 862.

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Diagnosis and Treatment of Hemodynamic Abnormalities after Acute Myocardial Infarction

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Care of patients in a Coronary Care Unit (CCU) has apparently reduced hospital mortality from acute myocardial infarction from 30% to 20%¹. This has been achieved almost exclusively by the prevention or prompt treatment of serious arrhythmias. The most frequent cause of death from acute myocardial infarction in the hospital is now failure of the heart as a pump, so called "power failure"². Cardiogenic shock, an arbitrarily defined end stage of the continuum of left ventricular dysfunction, has been particularly refractory to treatment. The use of vasoactive drugs such as nor-epinephrine and isoproterenol has not reduced significantly the 80 to 90% mortality rate encountered in this stage of hemodynamic abnormality³. If an impact is to be made new approaches to the treatment of the entire continuum of power failure must be devised.

At autopsy over 40% of the left ventricular mass is found to be infarcted in patients who die in cardiogenic shock. If we presume that any patient with an infarction of more than 40% of his left ventricular mass will not survive short of cardiac transplantation or use of an implantable artificial heart, therapeutic methods that are not practical at this time, those patients with power failure who

If the hemodynamic abnormalities are viewed as a continuum from normal pump function to severe power failure, potential problems may be appreciated earlier and more precise therapy instituted.

may be salvaged are those whose infarction has not yet involved 40% of their left ventricle. The therapeutic goal must therefore be to identify such patients and to preserve borderline areas of myocardium while maintaining cardiac performance sufficient for the needs of the body. In physiologic terms, adequate cardiac output must be maintained with the least possible increase in myocardial oxygen consumption ($\dot{MVO}_2$). Improved cardiac output and arterial pressure may in turn preserve myocardium by improving coronary perfusion. A vicious cycle, shock followed by more myocardial damage and thus more severe shock, may thereby be avoided.

Those factors that determine $\dot{MVO}_2$ are⁵: systolic blood pressure, ventricular radius, heart rate, systolic ejection time, and the state of myocardial inotropy (contractility). Classic treatment of hemodynamic abnormalities in acute infarction, especially shock,

consists primarily of the use of vasoactive agents. These drugs improve cardiac output and/or blood pressure at the expense of an increased $\dot{MVO}_2$ resulting from increased heart rate, blood pressure, or contractility. Since the coronary blood flow to at least some segments of the myocardium is severely limited in acute myocardial infarction, an increased $\dot{MVO}_2$ may compromise marginally perfused areas of myocardium and therefore increase infarct size⁶.

The destruction of left ventricular myocardium in patients with myocardial infarction results in a spectrum of clinical findings indicative of compromised pump function. A low systolic arterial pressure, a narrowed pulse pressure, cool skin and a declining urine flow reflect reduced cardiac output. The presence of a ventricular gallop sound and of pulmonary rales are usually indicative of elevated left ventricular filling pressure (LVFP). These findings are useful indices of the hemodynamic status of the patient but have proved to be unreliable at times in evaluating individual patients⁷.

Substantive data regarding myocardial performance began to appear with inauguration of the Myocardial Infarction Research Units (MIRU). However, it was not until Swan and Ganz developed the balloon tipped flow

HEMODYNAMIC ABNORMALITIES AFTER MYOCARDIAL INFARCTION

GORFINKEL, HAIDER AND LINDSAY

directed catheter that could be passed safely into the pulmonary artery at the bedside without the use of fluoroscopy in critically ill patients that these data could be widely applied clinically.

With this catheter right sided cardiac pressures, including pulmonary artery wedge pressure as an index of left ventricular filling pressure, can be measured and cardiac output obtained by the thermodilution technique. Since the introduction of this technique a spectrum of hemodynamic abnormalities in acute myocardial infarction has been precisely defined⁷. If the hemodynamic abnormalities are viewed as a continuum from normal pump function to severe power failure, potential problems may be appreciated earlier and more precise therapy instituted.

This paper will review: A) Clinical recognition of patients in whom bedside catheterization of the heart is useful. B) The hemodynamic subsets that comprise the spectrum of abnormalities in acute myocardial infarction. C) The forms of hemodynamic intervention which are useful.

A. Clinical recognition of patients in whom bedside catheterization is useful

Not all patients with acute myocardial infarction need hemodynamic study. In order to identify those patients in whom such an intervention is warranted certain clinical manifestations of three basic hemodynamic parameters must be evaluated. These are cardiac output, left ventricular filling pressure, and arterial blood pressure, which can be assessed as follows:

CARDIAC OUTPUT: Cardiac output may be equated with tissue perfusion. Cool skin, or cool and clammy skin, and peripheral cyanosis indicate reduced perfusion. A change in mental status or progressive obtundation is

indicative of reduced cerebral blood flow. Oliguria, less than 30 cc/hour, suggests diminished renal blood flow. If the patient has not voided within several hours of admission and any other indicators of altered hemodynamic function (as described above and to be described below) are present an indwelling bladder catheter should be inserted for accurate determination of urine volume.

ELEVATED LEFT VENTRICULAR FILLING PRESSURE (LVFP): Left ventricular end diastolic pressure or left ventricular filling pressure can be equated to left atrial pressure or pulmonary artery wedge pressure (PAWP). LVFP can be assessed by wheezing, dyspnea and orthopnea; by tachycardia, S-3 gallop, elevated venous pressure, rales and edema; by the laboratory findings of reduced arterial PO_2 ; and by the chest x-ray findings of pulmonary congestion⁹.

ARTERIAL BLOOD PRESSURE: Arterial blood pressure is assessed in the conventional manner with a sphyngomanometer, but in situations of intense vasoconstriction it may be difficult to obtain and may not reflect the central aortic pressure. In this situation direct arterial cannulation will be necessary.

If on sequential evaluation a combination of any of the above findings are present, the patient is a candidate for bedside hemodynamic study. Indication for study may be present on admission, or develop over a period of hours. In such patients falling arterial blood pressure (but still within the normal range), an increasing tachycardia, and a dwindling urine volume suggest deteriorating left ventricular function.

The central venous pressure has frequently been used to estimate cardiac filling pressures. Indeed, this measurement is often useful in abnormal hemodynamic states in which the heart is not primarily involved. Since

acute myocardial infarction predominantly damages the left ventricle, the central venous pressure may bear little relation to the left ventricular filling pressure¹⁰.

B. Hemodynamic subsets in acute myocardial infarction

Significant numbers of patients with acute myocardial infarction have now been studied by means of bedside catheterization. Cardiac output, arterial pressure and left ventricular filling pressure have been found to correlate with the clinical condition of the patient and with prognosis. Stroke work index (SWI), a derivation of cardiac output and arterial blood pressure, seems to be a reliable index of left ventricular pump function. When it is found to be 49 g-m/m² or more there is an almost zero mortality, with a stroke work index of 28 to 48 g-m/m² a mortality of 33% is encountered,¹¹ and a SWI of less than 25 g-m/m² is associated with a 94% mortality¹².

The hemodynamic findings after myocardial infarction are surprisingly variable. They may however be grouped into seven subsets (Figure 1). The following is a modification of a scheme of Chatterjee and Swan⁷.

Subset I—Normal SWI in relation to LVFP. These patients are uncomplicated. They can usually be identified clinically and thus do not warrant cardiac catheterization or specific therapy.

Subset II—Increased SWI in relation to LVFP. These patients will exhibit tachycardia and normal or elevated arterial pressure. Urine output is normal and signs of left heart failure are usually absent. They resemble other types of patients with excess catecholamine secretion and may benefit from beta-blocker therapy. This type of patient is seen relatively infrequently.

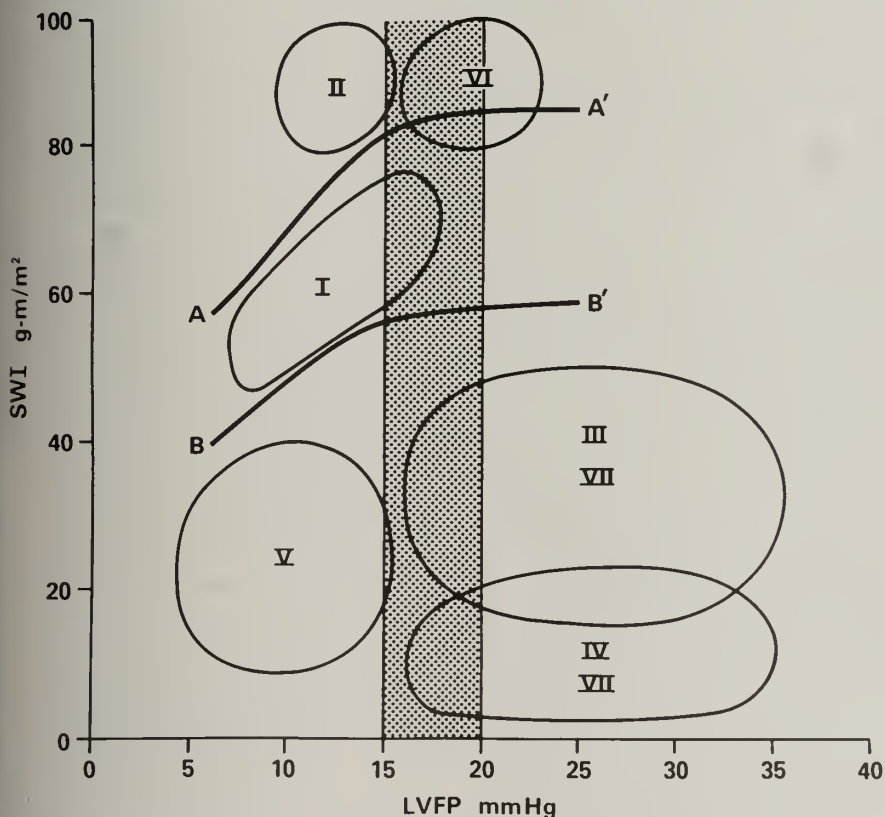


FIG. 1. Categorization of patients by subset according to stroke work index and left ventricular filling pressure. The shaded area represents the range of optimal left ventricular filling pressures. Lines A-A' and B-B' enclose the region of normal SWI response to a given filling pressure. I-VII—hemodynamic subsets.

Subset III—Reduced SWI with elevated LVFP without clinical evidence of shock. The largest number of patients with acute myocardial infarction fall into this category. Cardiac output and arterial pressure are slightly to moderately reduced, but evidence of severely compromised perfusion is lacking. Overt pulmonary edema on x-ray, an S-3 gallop, rales, and tachypnea are often but not invariably present. Arterial oxygen tension is decreased though not necessarily sufficiently to result in desaturation. Some patients in this category may later deteriorate into cardiogenic shock.

Subset IV—Markedly reduced SWI in relation to LVFP. These patients are those who manifest the "full blown" cardiogenic shock picture. They characteristically exhibit hypotension, cool and clammy skin, mental confusion and oliguria, and usually evidence of moderate or severe left ventricular failure. This is true although as a group their LVFP is not so high as patients with left ventricular failure who are not in shock.

Subset V—Reduced SWI with reduced or normal LVFP. These patients have low normal or hypotensive arterial blood pressure, may exhibit clinical evidence of hypoperfusion, but

characteristically do not manifest left ventricular failure^{1,3}. The reduced cardiac output in these patients may be improved with volume repletion. Difficulty may be encountered in separating them from others who, though not in obvious clinical left ventricular failure, would not benefit from fluid therapy. This is because clinical signs of left ventricular failure may be inapparent until the LVFP is well above 25 mm. Hg. Thus a patient with an LVFP of 23 mm. of Hg. probably would not benefit from volume expansion but might clinically be indistinguishable from a patient with an LVFP of 12 mm. Hg. who would benefit from such therapy. Right heart catheterization would clearly separate these two patients.

Two other distinctive groups of patients who may fall within this subset are noteworthy. Those with inferior infarction as a result of right coronary artery occlusion may also have involvement of the right ventricle and may present with hypotension, evidence of poor perfusion, and right ventricular failure¹⁴. Such patients manifest systemic venous engorgement without significant dyspnea or orthopnea. Right heart catheterization demonstrates elevated right atrial pressure, and frequently there is very little pressure change as the catheter is advanced from the right atrium to the right ventricle to the pulmonary artery. The pulmonary artery wedge pressure may be normal to moderately elevated. In this situation the infarcted right ventricle may be unable to generate sufficient pressure to adequately prime the left ventricle.

The second group consists of those patients who are hypotensive but who maintain a normal cardiac output and left ventricular filling pressure. These patients characteristically maintain an adequate urine volume and warm skin. Their SWI is reduced, mainly as a result of the reduced arterial pressure,

HEMODYNAMIC ABNORMALITIES AFTER MYOCARDIAL INFARCTION

GORFINKEL, HAIDER AND LINDSAY

not because of a reduced cardiac output. Such patients usually warrant no therapeutic intervention but bear close observation.

Subset VI—The patient who maintains severe hypertension (systolic arterial pressure more than 160 mm. Hg.) after exacerbating causes have been alleviated but who has no overt failure or findings of excessive catecholamine release (sweating, tachycardia) falls into this category. These patients may not warrant cardiac catheterization. Reduction of the elevated arterial pressure is essential and helps to reduce the ultimate size of the infarct.

Subset VII—Patients with mechanical defects as a result of their infarction. Hemodynamically these patients will usually fall into subsets III and IV but will in addition have findings of rupture of the ventricular septum or of a papillary muscle. Identification of these exacerbating factors is essential and may often be made by means of right heart catheterization. This is true even if surgical correction may not be advisable early in the course. The hemodynamic burden of these lesions may be reduced by vasodilator therapy or by counterpulsation¹⁵.

C. Hemodynamic Intervention

The various subsets and the type of therapy indicated within each subset is outlined in Table I (modified after Chatterjee and Swan⁷).

Therapeutic decisions cannot be arbitrarily made based upon the hemodynamic parameters. The response of any given patient may vary to therapy as compared to the group as a whole. Nonetheless, certain guidelines can be formulated. Moreover, a knowledge of the available therapeutic modalities as well as their potential benefits and hazards is essential for rational selection of therapy based upon the hemodynamic subsets.

I. Volume Loading

In the normal heart there are a number of mechanisms by which cardiac output may be increased. Most result in an increased $\dot{MVO}_2$. In the normal heart coronary blood flow increased proportionally to the increased energy requirements. Starling's law of the heart describes one of the mechanisms by which cardiac output may be increased¹⁶. It states that an increase in end diastolic volume of the ventricle results in an increase in stroke volume.

The beneficial effects of Starling's law may be recruited by means of volume expansion in power failure associated with acute myocardial infarction. This maneuver may increase left ventricular diastolic volume and may therefore improve output at low, normal, or even slightly elevated left ventricular filling pressures. Ventricular volume may be approximated by LVFP; though LVFP is determined by left ventricular wall compliance (stiffness) in addition to diastolic inflow and size of the ventricle. However,

over a short period of time a change in LVFP caused by increased inflow is a function of increased ventricular volume rather than a change in compliance. Though improving output by this mechanism will increase $\dot{MVO}_2$ to some extent, the beneficial effects of improved cardiac output and organ perfusion are worth the increased oxygen cost. This is particularly true if the improvement in output is achieved at a lower net increase in $\dot{MVO}_2$ than would be achieved with a comparable increase in cardiac output by means of inotropic agents.

Because of the close relationship between pulmonary artery wedge pressure and left ventricular filling pressure it is essential to monitor this pressure during volume loading to prevent worsening pulmonary congestion.

It has been determined that the optimal SWI is achieved in patients with acute myocardial infarction at a left ventricular filling pressure of 15 to 20 mm. Hg.¹⁷⁻¹⁸. Individual patients may vary, therefore each patient must serve as his own control. For example, a patient with an LVFP of 12 mm. Hg. would be expected to benefit from volume expansion, one with an LVFP of 19 mm. Hg. might or might not benefit, but a carefully monitored trial is often desirable.

II. Sympathomimetic Amines

Vasoactive drugs such as nor-epinephrine and isoproterenol have been used for years to increase cardiac output and/or blood pressure. They also produce a significant increase in myocardial oxygen consumption⁶. This probably accounts for the fact that they rarely reverse the shock syndrome permanently and have not substantially reduced the mortality of patients in that state. These agents have been shown experimentally to increase the infarct size, and therefore their use is limited.

TABLE I

Treatment of Hemodynamic Abnormalities
in Acute Myocardial Infarction
(modified after Swann & Chatterjee)⁷

Subset	Observation
Subset I	
Subset II	Beta blockers
Subset III	Impedance reduction, diuretics, digitalis
Subset IV	Impedance reduction, mechanical circulatory assistance
Subset V	Volume expansion
Subset VI	Impedance reduction (anti-hypertensive agents)
Subset VII	Mechanical circulatory assistance, impedance reduction, surgical correction

III. Impedance Reduction

It has recently been shown that controlled reduction in arterial pressure ("impedance reduction")¹⁹ in normotensive or slightly hypotensive patients with agents that can be controlled precisely (nitroprusside, phentolamine) can produce improvement in the clinical state. Improved cardiac output and tissue perfusion and a reduction in left ventricular filling pressure accompany a small decline in arterial blood pressure¹⁹⁻²¹. This intervention tends to reduce myocardial oxygen cost while improving the clinical picture. This can be viewed as an improvement in efficiency. Moreover, there is a suggestion that these agents may reduce the ultimate size of the infarct⁶. Impedance reduction seems potentially most beneficial in patients with elevated LVFP and systolic arterial pressures above 90-100 mm. Hg.

IV. Mechanical Assistance

The patient with full blown shock probably is not a candidate for impedance reduction alone since the arterial blood pressure is already low. Coronary perfusion is pressure dependent and severe reduction in arterial blood pressure is undesirable. Such patients may benefit from mechanical assistance such as counterpulsation,²² possibly combined with impedance reduction. Cardiac catheterization and coronary and left ventricular angiography²³ to locate any surgically remediable lesions may be performed¹⁵. Though a few patients may be salvaged with mechanical assistance alone, dramatic efforts seem justified since these patients have a greater than 90% mortality rate with current medical therapy²².

V. Diuretics

Diuretics are useful to free the lungs of fluid in patients with pulmonary edema and serve to improve the patient's comfort. In addition to its diuretic effect, furosemide initially lowers pulmonary blood volume and LVFP by increasing venous capacitance and thereby decreasing venous return. Thus the hemodynamic benefit begins before the diuresis occurs²⁴. Subsequently the diuresis produced by the drug augments the continued reduction of pulmonary blood volume and the lowering of LVFP²⁵.

Discretion must be maintained when using furosemide in patients who have severe left ventricular dysfunction and pulmonary edema. This is so because as the LVFP is lowered cardiac output may decline and hypotension ensue²⁵.

VI. Digitalis

The value of digitalis in acute myocardial infarction remains debatable²⁶. No clear cut benefits have been reported and its use in severe cardiogenic shock may even be deleterious²⁷. However, digitalis probably should be used when overt pulmonary edema complicates the picture.

Conclusion

It is most valuable to consider the diagnosis and treatment of hemodynamic derangements in acute myocardial infarction in relation to definable subsets determined by bedside hemodynamic evaluation. Hemodynamic abnormalities may be viewed as a spectrum rather than as specific syndromes. The concept of obtaining optimal hemodynamic improvement with the least increase in myocardial oxygen cost is stressed.

References

1. KILLIP T., KIMBALL J. T.: A survey of the coronary care unit: Concept and results. *Prog Cardiovasc Dis* 11: 45-52, 1968.
2. SWAN H. J. C., FORRESTER J. S., DIAMOND G., *et al*: Hemodynamic spectrum of myocardial infarction and cardiogenic shock. *Circulation* 45:1097-1110, 1972.
3. KUHN L. A.: Support of the circulation in acute myocardial infarction. *Mt. Sinai J Med* 37:297-310, 1970.
4. PAGE D. L., CAULFIELD J. B., KASTOR J. A., *et al*: Myocardial changes associated with cardiogenic shock. *New Eng J Med* 285:133-137, 1971.
5. BRAUNWALD E.: Control of myocardial oxygen consumption. *Amer J Cardiol* 27:416-432, 1971.
6. MAROKO P. R., BRAUNWALD E.: Modification of myocardial infarction size after coronary occlusion. *Annals Int Med* 79:720-733, 1973.
7. CHATTERJEE K., SWAN H. J. C.: Hemodynamic profile of acute myocardial infarction, in *Myocardial Infarction*, Eds. Corday E and Swan HJC, Williams and Wilkins Co. Publishers, 1973, pps. 51-61.
8. SWAN H. J. C., GANZ W., *et al*: Catheterization of the heart in man with use of a flow directed balloon tipped catheter. *New Eng J Med* 283:447-451, 1970.
9. ROTMAN M., CHEN J. T. T., SENINGEN R. P., *et al*: Pulmonary artery diastolic pressure in acute myocardial infarction. *Amer J Cardiol* 33:357-362, 1974.
10. RAPAPORT E., SCHEINMAN M.: Rationale and limitations of hemodynamic measurements in patients with acute myocardial infarction. *Mod Concept of Cardiovasc Dis* 38:55-61, 1969.
11. HAMOSH P., COHN J. N.: Left ventricular function in acute myocardial infarction. *J Clin Invest* 50:523-533, 1971.
12. PRAKASH R., FORRESTER J., PARMLEY W. W., *et al*: Prognostic implications of left ventricular stroke work index in acute myocardial infarction. *Clin Res* 20:391, 1972.
13. LOEB H. S., PIETRAS R. J., TOBIN J. R., *et al*: Hypovolemia in shock due to acute myocardial infarction. *Circulation* 40:653-659, 1969.

HEMODYNAMIC ABNORMALITIES AFTER MYOCARDIAL INFARCTION

GORFINKEL, HAIDER AND LINDSAY

14. COHN J. N., GUIHA N. H., BRODER M. I., *et al*: Right ventricular infarction. *Amer J Cardiol* 33:209-214, 1974.
15. MUNDTH E. D., BUCKLEY M. J., LEINBACH R. C., *et al*: Surgical intervention for the complications of acute myocardial ischemia. *Ann Surg* 178:379-390, 1973.
16. FRIEDBERG C. K.: *Diseases of the Heart*. W. B. Saunder Co., Publishers, 1966; p. 139.
17. RACKLEY C. E., RUSSELL R. O., JR.: Left ventricular function in acute myocardial infarction and its clinical significance. *Circulation* 45: 231-244, 1972.
18. CREXELLS C., CHATTERJEE K., FORRESTER J. S., *et al*: Optimal level of filling pressure in the left side of the heart in acute myocardial infarction. *New Eng J Med* 289:1263-1266, 1973.
19. COHN J. N.: Editorial: Vasodilator therapy for heart failure. *Circulation* 48:5-8, 1973.
20. CHATTERJEE K., PARMLEY W. W., GANZ W., *et al*: Hemodynamic and metabolic responses to vasodilator therapy in acute myocardial infarction. *Circulation* 48:1183-1193, 1973.
21. FRANCIOSA J. A., GUIHA N. H., LIMAS C. J., *et al*: Improved left ventricular function during nitroprusside infusion in acute myocardial infarction. *Lancet* 1:650-654, 1972.
22. SCHEIDT S., WILNER G., MUELLER H., *et al*: Intra-aortic balloon counterpulsation in cardiogenic shock. *New Eng J Med* 288:979-984, 1973.
23. LEINBACH R. C., GOLD H. K., DINSMORE R. E., *et al*: The role of angiography in cardiogenic shock. *Circulation (Supplement II)* 48:III-95-98, 1973.
24. DIKSHIT K., VYDEN J. K., FORRESTER J. S., *et al*: Hemodynamic effects of furosemide in cardiac failure. *New Eng J Med* 288:1087-1090, 1973.
25. MOND H., HUNT D., SLOMAN G.: Haemodynamic effects of furosemide in patients suspected of having acute myocardial infarction. *Brit Heart J* 36:44-53, 1974.
26. KARLINER J. S., BRAUNWALD E.: Present status of digitalis treatment of acute myocardial infarction. *Circulation* 45:891-902, 1972.
27. COHN J. N., TRISTANI F. E., KHATRI I. M.: Cardiac and peripheral vascular effects of digitalis in clinical cardiogenic shock. *Amer Ht J* 78:318-330, 1969.

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A Case Report of *Serratia* Endocarditis with Review of the Literature

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Abstract

A case of *Serratia marcescens* endocarditis involving the pulmonary valve in a heroin addict is presented. To our knowledge, this is the first reported case of pulmonary valve endocarditis caused by *Serratia marcescens* and the only one to be treated medically with success. Review of the twelve previously published cases of endocarditis caused by this organism reveals that this disease has a very high mortality rate and should be treated vigorously with Gentamicin and Carbenicillin if antibiotic tube dilution studies show synergetic effect against this bacteria.

Although the first report of infection due to *Serratia marcescens* was published in 1913 by Woodward¹, it was not until recently that the pathogenic potential of this micro-organism under certain clinical conditions received reasonable attention. *Serratia marcescens* is a gram-negative motile rod belonging to the group of Klebsiella-Enterobacter-Serratia, once believed to be non-pathogenic². It is now apparent that these bacteria are capable of producing severe infections of the respiratory tract, urinary tract, and of wounds and tissues with septicemia and endocarditis. Since 1960, there has been increasing interest in infections caused by pigmented and non-pigmented *Serratia marcescens*. Isola-

tion of this gram-negative enterobacterium from clinical specimens has become more frequent³⁻⁵ and there have been reports of outbreaks of hospital-acquired infections⁶⁻¹¹.

Only twelve previous cases^{1,2,22} of *Serratia marcescens* endocarditis have been described. The subject of this paper is the thirteenth case and to our knowledge, the first case report of pulmonary valve involvement by this bacterium. It is also the first such case successfully treated with a combination of Gentamicin and Carbenicillin.

Case Report:

A. E., a 42-year-old black man, a known heroin addict for 20 years, was admitted to the District of Columbia General Hospital on May 12, 1972, because of malaise and weakness for four weeks, followed by chills and fever for two weeks prior to admission. For two years prior to admission he had been skin popping because of the extensive scarring of the veins. His last heroin injection was two months prior to admission. The patient denied cough, chest pain or shortness of breath. His past history was unremarkable except for an admission to this hospital in 1955 for drug rehabilitation. There was no history of rheumatic fever or heart disease.

Physical examination showed a de-

Review of the twelve previously published cases of endocarditis caused by *Serratia marcescens* shows that this disease has a very high mortality rate and should be treated vigorously with Gentamicin and Carbenicillin if antibiotic tube dilution studies show synergetic effect against this bacteria.

hydrated man in moderate distress with a temperature of 104°F., a pulse 100 per minute, respirations of 20 per minute, and a blood pressure of 130/75 mm Hg. The conjunctiva and mucous membranes were pale. Examination of the cardiovascular system showed a grade 3/6 diastolic murmur best heard at the second left intercostal space parasternally. The murmur increased during inspiration. The liver was palpable 2 finger-breadth below the right costal margin. The tip of the spleen was palpable on deep inspiration. There was extensive scarring of both hands, forearms and arms, but there were no petechiae, splinter hemorrhages or Roth spots.

Laboratory data on admission showed a white blood count of 17,100/cmm, hematocrit of 19.6%, hemoglobin of 6.6 gms%; the urinalysis showed one plus protein and many red

SERRATIA ENDOCARDITIS

FARHOUDI, BANKS AND ALI

blood cells. The blood urea nitrogen (BUN) was 52 mg%, electrolytes and creatinine were within normal limits. The chest x-ray (Fig. 1) showed multiple nodular densities in both lung fields.

A diagnosis of infective endocarditis was made and he was started on Penicillin G., 12 million units daily. On the third hospital day, all six blood cultures drawn on admission were reported to grow gram-negative rods.

Four more blood cultures were obtained and the patient was switched to Gentamicin 5 mg/kg/24 hours in three divided doses intramuscularly. On the next hospital day the gram-negative rods were identified as *Serratia marcescens*, which was sensitive only to Kanamycin, Gentamicin, Chloramphenicol and Carbenicillin by disc sensitivity technique. Tube dilution studies showed (Table I) that the combination of Gentamicin and Carbenicillin had a synergistic effect. The serocidal level, one hour before the administration of the next Gentamicin dose was at 1:4 dilution. Carbenicillin 40 gms. intravenously daily in four divided doses was added to the antibiotic regimen on the fourth hospital day. The four additional blood cultures and a sputum culture, which had been obtained while the patient was on Penicillin, were positive for *Serratia marcescens*.

The patient became afebrile two days after the combination therapy. Although subsequent blood cultures remained negative, he started to spike temperatures to 100-101°F. daily, one week later. Because of the high minimum bacteriocidal level of Gentamicin it was decided to increase this antibiotic to 6.75 mg/kg/24 hours in four divided doses intravenously. The patient's BUN returned to normal by the fifth hospital day and serial electrolytes, creatinine, BUN, creatinine clearance and audiometry studies stayed within normal limits. Phonocardiogram showed a crescendo-decrescendo diastolic murmur, best recorded in the pulmonary area. The murmur started with the pulmonic component of the second heart sound and increased during inspiration.

Gentamicin and Carbenicillin were continued for six weeks. The patient became afebrile during the third hospital week and was kept under observation for seven weeks following discontinuation of therapy. He showed no



FIG. 1. AP view of chest x-ray shows multiple nodular densities bilaterally.

TABLE I

Antibiotic Tube Dilution Sensitivity with Gentamicin, Tobramycin and Carbenicillin against *Serratia Marcescens*

	Gentamicin mcg/ml	Tobramycin mcg/ml	Carbenicillin mcg/ml	Gentamicin and Carbenicillin mcg/ml
MIC*	3.12	25	50	1.6 G. 6.25 C.
MBC†	12.5	50	200	3.12 G. 12.5 C.

* MIC: Minimum Inhibitory Concentration

† MBC: Minimum Bacteriocidal Concentration

G: Gentamicin

C: Carbenicillin

evidence of recurrence of endocarditis and was discharged on August 4, 1972.

Discussion:

Contrary to the previous belief, it is increasingly evident that *Serratia marcescens*, a member of the gram-negative *Enterobacteriaceae* which are found naturally in water, soil and certain foods^{2,3}, does indeed cause infections, some of them quite serious. The great majority of strains do not produce pigment and easily may be mistaken for other species of *Enterobacter*.

Serratia infections are likely to occur in the elderly, those with chronic debilitating disorders, in hospitalized patients and especially in those with a predisposing factor^{2,4} such as treatment with broad spectrum antibiotics or corticosteroids and instrumentation of the genitourinary and respiratory tracts. Most infections caused by this bacteria are hospital-acquired and are associated with altered host resistance, as has been emphasized in recent years⁶⁻¹¹.

Serratia marcescens septicemia carries a high mortality^{4,12-25}. Wilkowske and his associates²² reviewed

ten such cases of whom only two survived. One of the survivors had a transient bacteremia which led the authors to believe that the patient could have had a contaminated blood culture rather than true septicemia. Altemier et al²⁵ reported a 40% mortality rate in forty-two patients.

To our knowledge only twelve cases of *Serratia* endocarditis have previously been reported^{1,2-22} (Table II). It is clear that open heart surgery and previous treatment with multiple antibiotics are the two most important predisposing factors in this group of patients. Five out of thirteen patients had infection of prosthetic heart valve and had received multiple antibiotics. Three patients (including ours) were heroin addicts.

Endocarditis due to gram-negative bacteria and especially that due to *Serratia marcescens* is quite uncommon. Gram-negative bacteria account for only 1-3% of the reported cases of endocarditis^{2,6}. The rarity of the right-sided endocarditis^{2,7-28} is well known. The lack of involvement of the right side of the heart in this group (Table II) may be more apparent than real if it is kept in mind that five out of nine with left-sided endocarditis

had cardiac surgery on that side. Two out of three heroin addicts had involvement of the right side of the heart. This is in agreement with the previous reports of predominance of the right-sided endocarditis in heroin addicts, at least in the Washington Metropolitan area^{2,9-31}. It should be stressed, however, that even with the sharp increase in gram-negative endocarditis in recent years, *Staphylococcus aureus* (coagulase positive) still remains the most common organism causing septicemia and endocarditis among narcotic addicts^{2,9-34}.

Although there have been previous case reports of pulmonary valve endocarditis due to *Staphylococcus aureus*, coagulase positive³⁵, to our knowledge this is the first case of *Serratia marcescens* involving this valve. The rarity of endocarditis of the pulmonary valve can best be explained by the lower hemodynamic pressures on the right side of the heart. The bacteria should be overwhelming virulent to cause infection, as is the case for *Staphylococcus aureus*. The infection of the pulmonary valve due to *Serratia marcescens*, which has a low pathogenicity, is interesting. Our case demonstrated the typical clinical features of pulmonary regurgitation and septic emboli to the lungs (Fig. 1). The phonocardiogram clearly shows the diastolic murmur starting from the second component of the second heart sound in the pulmonary area.

Serratia endocarditis has a very high mortality rate. Only three (including this case) out of thirteen reported patients survived. Even in these three cases it is doubtful if case number eight (Table II) reported by Quintiliani and Gifford¹⁸ had genuine endocarditis. This patient was a 50-year-old man with a known history of previous myocardial infarction who was admitted to the hospital with chest pain and a low pitched systolic murmur along the left sternal border. The

SERRATIA ENDOCARDITIS

FARHOUDI, BANKS AND ALI

TABLE II

Endocarditis Due to *Serratia Marcescens*

Case No.	Reference Author	Patient's Age and Sex	Predisposing Factor(s)	Valvular Involvement	Treatment	Outcome
1.	Wheat et al (12)	67, M.	Indwelling urinary catheter	Tricuspid	Penicillin Streptomycin Chloramphenicol	Died
2.	Hawe and Hughes (13)	38, M.	Multiple antibiotics, urinary tract infection	Mitral	Chloramphenicol	Died
3.	Reissell and Jansson (14)	41, F.	Narcotic Addict	Aortic, Mitral	Penicillin, Streptomycin	Died
4.	Denny and Kaye (15)	59, F.	Recent dental procedures	Mitral	Kanamycin, Sulfadiazine	Died
5.	Amoury and Bowman (16)	35, M.	Cardiac surgery, Starr-Edwards Prosthesis, tricuspid valvuloplasty	Aortic?	Chloramphenicol, Ampicillin	Died
6.	Alexander et al (17)	46, M.	Cardiac surgery, homograft replacement of aortic valve, multiple antibiotics	Aortic	Sodium Colistimethate, Sodium Cephalothin	Died
7.	Quintiliani and Gifford (18)	64, F.	Infected polyethylene canula, prosthetic heart valves, multiple antibiotics	Tricuspid, Mitral	Kanamycin, Chloramphenicol, nalidixic acid I.V.	Died
8.	Quintiliani and Gifford (18)	50, M.	Arteriosclerotic heart disease, intravenous heparin therapy	?	Kanamycin, Chloramphenicol, Ampicillin	Survived
9.	Williams and Johnson (19)	71, F.	Abdominal surgery, partial colectomy, tracheostomy, multiple antibiotics	Mitral	Kanamycin, Sodium Cephalothin	Died
10.	Suri et al (20)	42, M.	Cardiac surgery, Cross-Jones mitral valve prosthesis, multiple antibiotics	Mitral	Methicillin, Penicillin, Cephaloridine, Ampicillin Chloramphenicol	Died
11.	Alexander et al (21)	24, F.	Drug addict	Tricuspid	Kanamycin, Chloramphenicol, Sulfisoxazole Nalidixic acid, Tricuspid valvulotomy	Survived
12.	Wilkowske et al (22)	?	Cardiac Surgery, Prosthetic aortic valve, multiple antibiotics	Aortic	Kanamycin Sulfate	Died
13.	Farhodi et al	42, M.	Drug addict	Pulmonary	Gentamicin, Carbenicillin	Survived

patient was given intravenous heparin through an indwelling scalp vein needle and heparin lock. Three days later he started to have chills and fever and his blood cultures grew *Serratia marcescens*. His blood cultures became negative shortly after removal of the needle. Culture from the tip of the needle was not made. We think that this patient had bacteremia and not endocarditis. The second survivor, case number eleven (Table 2) had to undergo surgical debridement of the tricuspid valve after unsuccessful prolonged, intensive, multiple antibiotic treatment and, therefore, represents a surgical rather than medical cure. The third survivor is the subject of this communication and to our belief the only case of *Serratia* endocarditis cured medically and the only reported case treated with Gentamicin and Carbenicillin.

Serratia are known to be resistant to many antibiotics. Because of the production of cephalosporinase they are usually resistant to cephalosporins^{3,6} and are sensitive to Chloramphenicol, Kanamycin and Gentamicin. The bacterial isolates from the blood of our patient were resistant to most antibiotics, except to Kanamycin, Chloramphenicol, Gentamicin and Carbenicillin. The inhibitory zone on disc sensitivity technique was greatest for Gentamicin. This is in agreement with the results reported by others^{4,22,23}. It is evident from the antibiotic tube dilution technique (Table 1) that the organism appears to be resistant to Tobramycin, a new aminoglycoside antibiotic with a gram-negative spectrum with special effectiveness for *Pseudomonas*³⁷⁻³⁸. Unfortunately, there have not been adequate of in-vitro studies of this antibiotic against *Serratia*. Greenfield and Feingold³⁹ reported a synergistic action of sulfanamides and polymyxins. However, there have been no clinical data to support their *in-vitro* studies. Re-

cently, Digout et al⁴⁰ reported in-vitro sensitivity of *Serratia* to Gentamicin and Carbenicillin. They found that 100 per cent of strains were susceptible to 10 mcg/ml of Gentamicin and 87.1% were sensitive to 100 mcg/ml of Carbenicillin. They did not test the combination of these antibiotics against the organism to find out if there was any synergistic action as is usually the case against *Pseudomonas aeruginosa*⁴¹⁻⁴². This is important. Although the minimum inhibitory concentration for Gentamicin in our patient was 3.12 mcg/ml, the minimum bacteriocidal concentration was 12.5 mcg/ml. One should be aware of the fact that the safe blood level of Gentamicin is usually below 10-12 mcg/ml. Had it not been for the synergistic effect of Carbenicillin and Gentamicin against *Serratia* in this case, he probably would not have been cured with the usual dosage of Gentamicin. Because of the difficulty in treatment of *Serratia* endocarditis, it is, therefore, extremely important to perform antibiotic tube dilution for individual antibiotics and their combinations for the most effective therapy. It is also necessary to obtain the serocidal level of antibiotic to assure if adequate blood level has been attained. Finally, it appears that the combination of Gentamicin and Carbenicillin, if given adequately, for a period of six weeks, is the treatment of choice for *Serratia marcescens* endocarditis.

References

1. WOODWARD, H. M., CLARK, K. B.: A Case of Infection in Man by the Bacterium prodigiosum. Lancet, 1:314-315, 1913.
2. MCENTEGART, M. G., PORTERFIELD, J. S.: Bacteremia Following Dental Extraction. Lancet, 2:596-598, 1949.
3. CLAYTON, E., VON GRAEVENITZ, A.: Non-pigmented *Serratia marcescens*. JAMA, 197:1059-1064, 1966.
4. WILFERT, J. N., BARRETT, F. F., KASS, E. H.: Bacteremia Due to *Serratia marcescens*. New Eng. J. Med., 279:286-289, 1968.
5. MAGNUSON, C. W., ELSTON, H. R.: Infections Caused by Non-pigmented *Serratia*. Ann. Intern. Med., 65:409-418, 1966.
6. MCCORMACK, R. C., KUNIN, C. M.: Control of a Single Source Nursery Epidemic Due to *Serratia marcescens*. Pediatrics, 37:750-755, 1966.
7. BURDIN, J. C., LOCHARD, J., SCHACK, F., et al: [Epidemic of Pleuropulmonary Infection Due to *Serratia marcescens* in a Hospital] (Fr.). Presse Med., 75:466-468, 1967.
8. RINGROSE, R. E., MCKOWN, B., FELTON, F. G., et al: A Hospital Outbreak of *Serratia marcescens* Associated with Ultrasonic Nebulizers. Ann. Intern. Med., 69:719-729, 1968.
9. CABRERA, H. A.: An Outbreak of *Serratia marcescens*, and its Control. Arch. Intern. Med., (Chicago), 123:650-655, 1969.
10. SAMUEL, D. A., CONGER, K. B.: *Serratia marcescens* Infection of the Urinary Tract: A Nosocomial Infection. J. Urology, 101:621-623, 1969.
11. SANDERS, JR., C. V., LUBY, J. P., JOHANSON, JR., W. G., et al.: *Serratia marcescens* Infections from Inhalation Therapy Medications: Nosocomial Outbreak. Ann. Intern. Med., 73:15-21, 1970.
12. WHEAT, R. P., ZUCKERMAN, A., RANTZ, L. A.: Infections Due to Chromobacterium: Report of 11 Cases. Arch. Intern. Med., 88:461-466, 1951.
13. HAWES, A. J., HUGHE, M. H.: Bacterial Endocarditis Due to Chromobacterium prodigiosum. Brit. Med. J., 1:968-970, 1954.
14. REISSELL, P., JANSSON, E.: *Serratia marcescens* Septicemia. Acta Med. Scand., 176:253-256, 1964.
15. DENNEY, J. D., KAY, D., HAGSTROM, J. W. C.: Endocarditis Due to *Serratia marcescens*. New Eng. J. Med., 276:1362, 1967.
16. AMOURY, R. A., BOWMAN, JR., F., MALM, J. R.: Endocarditis Associated with Intracardiac Prostheses: Diagnosis, Management and Prophylaxis. J. Thorac Cardiovasc. Surg., 51:36-47, 1966.
17. ALEXANDER, R. H., REICHENBACH, D. O., MERENDINO, K. A.

SERRATIA ENDOCARDITIS

FARHOUDI, BANKS AND ALI

- Serratia marcescens* Endocarditis. Arch. Surg., 98:287-291, 1969.
18. QUINTILIANI, R., GIFFORD, R. H.: Endocarditis from *Serratia marcescens*. JAMA, 208:2055-2059, 1969.
 19. WILLIAMS, JR., J. C., JOHNSON, J. E.: *Serratia marcescens* Endocarditis, Report of a Patient. Arch. Intern. Med., 125:1038-1040, 1970.
 20. SURI, R. K., Selby, D. A. HAWKS, G. H., *et al*: *Serratia marcescens* Endocarditis: A Report of a Case Involving Cross-Jones Mitral Valve Prosthesis, with a Review of the Literature. C.M.A. Journal, 104:1013-1014, 1971.
 21. ALEXANDER, R., HOLLOWAY, JR., G. A. HONSINGER, JR., R. W.: Surgical Debridement for Resistant Bacterial Endocarditis. JAMA, 210:1757-1759, 1969.
 22. WILKOWSKIE, C. J., WASHINGTON, II, J. A., MARTIN, W. J., RITTS, JR., R. E. *Serratia marcescens*, Biochemical Characteristics, Antibiotic Susceptibility Patterns and Clinical Significance. JAMA, 214:2157-2162, 1970.
 23. EICKHOFF, T. C., STEINHAEUER, B. W., FINLAND, M.: The Klebsiella-Enterobacter-Serratia Division. Ann. Intern. Med., 65:1163-1194, 1966.
 24. DODSON, W. H.: *Serratia marcescens* Septicemia. Arch. Intern. Med., 121:145-150, 1968.
 25. ALTEMEIER, W. A., CULBERTSON, W. R., FULLER, W. D., *et al*: *Serratia marcescens* Septicemia in Surgical Patients. Arch. Surgery (Chicago), 99:232-238, 1969.
 26. LERNER, P. I., WEINSTEIN, L.: Infective Endocarditis in the Antibiotic Era. New Eng. J. Med., 274:199-206, 1966.
 27. BAIN, R. C., EDWARDS, J. E., Scheifley, C. H., GERACI, J. E.: Right-sided Bacterial Endocarditis and Endarteritis. Am. J. Med., 24:98-110, 1958.
 28. BASHOUR, F. A., WINCHELL, C. P.: Right-sided Bacterial Endocarditis. Am. J. M. Sc., 240:411-416, 1960.
 29. HUSSEY, H. H., KATZ, S.: Infections Resulting from Narcotic Addiction: Report of 102 Cases. Am. J. Med., 9:186-193, 1950.
 30. OLSSON, R. A., ROMANSKY, M. J.: Staphylococcal Tricuspid Endocarditis in Heroin Addicts. Ann. Int. Med., 57:755-762, 1962.
 31. FARHOUDI, H. O., MODY, V. R.: Staphylococcal Bacteremia in Heroin Addicts. Med. Ann. D.C., 39:187-194, 1970.
 32. LOURIA, D. B., HENSLE, T., ROSE, J.: The Major Medical Complications of Heroin Addiction. Ann. Int. Med., 67:1-22, 1967.
 33. CHERUBIN, C. E.: The Medical Sequelae of Narcotic Addiction. Ann. Int. Med., 67:23-33, 1967.
 34. OETHER, F. J., GOODMAN, J. L., LERNER, A. M.: Infections in Paregoric Addicts. JAMA, 190:683-686, 1964.
 35. MASSUMI, R. A., JUST, H., TAWAKOL, A.: Pulmonary Valve Regurgitation Secondary to Bacterial Endocarditis in Heroin Addicts. Am. Heart J., 73:308-316, 1967.
 36. FLEMING, P. C., GOLDNER, M., GLASS, D. G.: Observation on the Natural Distribution and Significance of Cephalosporinase. Lancet, 1:1399-1401, 1963.
 37. SHADOMY, S. In Vitro Studies with Tobramycin. Clinical Research, 20:83, January, 1972.
 38. TRAUB, W. H., Raymond, E. A.: Evaluation of the In Vitro Activity of Tobramycin as Compared with that of Gentamicin Sulfate. Applied Microbiology, 23:No. 1, January, 1972.
 39. GREENFIELD, S. FEINGOLD, D. S.: The Synergistic Action of the Sulfonamides and the Polymyxins Against *Serratia marcescens*. J. Inf. Dis., 121:555-558, 1970.
 40. DIGOUT, G. MACDONALD, S. VAN ROOYEN, C. E.: Sensitivity of *Serratia* to Gentamicin and Carbenicillin. N.S. Med. Bull., 50:79-81, 1971.
 41. ANDRIOLE, V. T. Synergy of Carbenicillin and Gentamicin in Experimental Infection with *Pseudomonas*. J. Inf. Dis., 124:S46-S55, 1971.
 42. YOUNG, L. S. Gentamicin: Clinical Use with Carbenicillin and In Vitro Studies with Recent Isolates of *Pseudomonas aeruginosa*. J. Inf. Dis., 124:S202-S206, 1971.

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SPECIAL ARTICLE

Causes of Death Soon After Injury*

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The necessity of preparing for accident victims should be obvious when we look at the near 55.7 million (Table 1) injuries occurring annually in this country. More than 117,000 deaths result from injury and near 11 million persons are disabled¹. The annual cost from wage loss, medical and insurance expenses exceeds 23.5 billion dollars.

In the District of Columbia², (Table 2) accidents, excluding homicide and suicide, were the fifth leading cause of death in 1970 and 1972. By sex and race, blacks and males compose 70% of the victims. If we (Table 3) combine accidents with other violence we see that these would represent the third leading cause of death, with motor vehicle deaths and homicide leading each subcategory. Motor vehicle deaths compose nearly 40% of accidents and homicide contributes more than 60 per cent of deaths from other violence.

It is probable that a downward trend in motor vehicle and homicide deaths will result from legislation directed at safer vehicles and better

TABLE 1	
Annual Trauma in the U.S.A. National Safety Council—1973	
Injuries	55.7 Million
Deaths	117,000
Disabled	11 Million
Vehicle injuries	56,600
Wage loss, medical and insurance cost	23.5 Billion

TABLE 2		
District of Columbia Deaths		
	1970	1972
Total	8,690	8,313
Heart	2,883	2,527
Cancer	1,488	1,482
CVA	663	698
Influenza	424	325
& pneumonia		
Cirrhosis		444
Accidents	417	329
		232 (M)
		233 (B)

TABLE 3			
D.C. Deaths from Major Trauma			
	1970	1971	1972
Accidents	417	349	329
Motor vehicle		132	
Accidental falls		83	
Burns, fire & flame	62	49	33
Other violence	336		439
Homicide	207		258
Suicide	70		94
Undetermined	59		87

TABLE 4	
D.C. Motor Vehicle Deaths 1972	
Total	98 (69)
Coll. pedestrian	35
Coll. vehicle	30
Non collision	19
loss of control	
Other collision	6
Unspecified	8

gun control laws. The decreasing deaths due to fire and flame burns appear to be related to fewer burns from clothing fires, as this was the major drop in this category from 1970 to 1972². More will have to be done with pedestrians, however, (Table 4) if the

deaths involving surface ambulatory traffic is to be decreased.

When death results from trauma within the first 24 hours, the offending agent of force generally causes irreparable damage to one or more vital organs, such as the brain, chest,

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CAUSES OF DEATH SOON AFTER INJURY

FUNDERBURK

lungs or great vessels^{3,4,5,6}. These patients generally present one or more of the following clinical syndromes: coma, hemorrhagic or cardiogenic shock^{3,6,7}. Approximately two thirds of patients dying from trauma die within the first 24 hours^{3,7}.

Death is usually instantaneous when there is massive damage to the brain. Hemorrhage and brain damage probably account for more than 50 per cent of deaths within the first 6 hours^{3,8}. In general persons with massive hemorrhage dying of exsanguination rarely live beyond 30 minutes⁸. This is one of the dominant reasons why more than 10% of major victims are dead on arrival to emergency care facilities³. The most critical time for reversal of injurious effects of major trauma is within the first 2-3 hours. It is because of this critical time period that appropriate first aid needs to be instituted, adequate medical services made available, and rapid decisive measures taken to reverse continuing injury⁹.

It is likely that near 20% of deaths related to trauma could be prevented if we resolved these problems of initial care;³ poor communication, inadequate or inappropriate first aid, badly trained ambulance drivers, inadequate portable emergency equipment and poor emergency room facilities. The delaying hazards of surface transportation are worsened by chance and intentional visitors. It would probably be more expeditious to arrange helicopter evacuation for congested or inaccessible areas because of innate curiosity which contributes to accident scene congestion.

The contribution of early evacuation is very apparent when we see its influence on deaths in combat (Table 5). Using helicopter evacuation, in the Korean and Vietnam War, the mortality rate was reduced by nearly 50%⁸. The further reduction in the Vietnam War deaths is better evidenced in the

ratio of battle field to hospital deaths, which suggest that 20% more casualties were able to get to the hospital and avoid death on the battle field. For patients sustaining abdominal injury, (Table 6) requiring surgery, time is again very important. If surgery is performed within six hours, the mortality is one half that delayed for 24 hours⁸.

As a general rule, patients who die within 24 hours following trauma have severe brain or brain stem injury, or severely crushed chest, cardiac rupture or major abdominal (Table II) or vascular injuries³. Those survivors usually do not have serious abdominal injury and brain injuries are mild^{3,6}.

TABLE 5

Combat Deaths Decreased in Relation
to Helicopter Transport

Conflict	Hospital Deaths (%)	Ratio Hospital to Battlefield Deaths
WWI	8	
WWII	4.5	1:4
Korean	2.5	1:4
Vietnam	2.5	1:5

CINCPAC # (War surgery manual) 1971
Commander-in-Chief Pacific

TABLE 6

Influence of Time on Mortality
Combat Abdominal Wounds

Time Lapse (Hrs) Injury—Surgery	Mortality Percent
6	8
12	12
24	16

References

1. National Safety Council. Accident Facts, 1973 Edition, Chicago.
2. MORSE, WARREN: Statistics and Evaluation Division, Department of Human Resources, D. C. Government, Personal Communication.
3. BOYD, D. R., FLASHNER, B. A., NYHUS, L. M., PHILLIPS, C. W.: Clinical and Epidemiologic Characteristics of Non-surviving Trauma Victims in an Urban Environment. *Journal of National Medical Association* 64: 1-7, 1972.
4. HUELKE, DONALD F.: Mechanism of Injury in Automobile Crashes, *California Med.* 116: 23-29, 1972.
5. HUNT, THOMAS K.: Triage, *Ariz. Med.* 26: 139-140, 1969.
6. CARTER, J. H., BURDGE, R., POWERS, S. R., Jr., CAMPBELL, C. J.: An Analysis of 17 Fatal and 31 Non-fatal Injuries Following an Airplane Crash. *The Journal of Trauma* 13: 346-352, 1973.
7. REYNOLDS, B. M., BALSANO, N. A., REYNOLDS, F. X.: Falls from Heights—A surgical experience of 200 consecutive cases. *Ann. of Surg.* 174: 304-308, 1971.
8. NELSON, T. G. Col. WRAMC, Personal Communication.
9. LLOYD, J. W., MONAHAN, P. R. W., BRIGGS, M., HIGGINS, G., WILLIAMS, D. G.: The Management of the patient with severe multiple injuries. *Brit. Jour. of Oral Surg.* 9: 73-76, 1971.

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Hypertensive Cerebellar Hemorrhage

WILLIAM H. LAWRENCE, M.D.

Abstract

Hypertensive cerebellar hemorrhage is difficult to diagnose on clinical grounds even when considered in the patient who presents with obtundation. Fluctuating blood pressure and characteristic bobbing eye movements may suggest the correct diagnosis. Two patients who illustrate these clinical signs are described.

Spontaneous Intracerebellar Hemorrhage accounts for 5-10% of all intracranial bleeding.¹ It may not be recognized unless included in the differential diagnosis of all hypertensive patients with stroke particularly where focal signs are absent. Obtundation which may be intermittent is often wrongly attributed to hypertensive encephalopathy or is considered a side effect of antihypertensive medications. Prompt diagnosis and surgical removal of clot before irreversible brain stem compression occurs is essential. Untreated, the mortality averages 75%.¹ The following two cases illustrate several signs which if present may strongly suggest the diagnosis.

Case 1

A 47 year old black man with a ten year history of intermittently treated hypertension developed a headache

Obtundation which may be intermittent is often wrongly attributed to hypertensive encephalopathy or is considered a side effect of antihypertensive medications. Prompt diagnosis and surgical removal of the clot is essential.

five days before admission which became intensified during intercourse and was accompanied by dyspnea. On admission he was in pulmonary edema with a blood pressure of 250/140 mm Hg and a pulse of 74 per minute. He was fully alert and neurologically intact. Apresoline and Lasix were administered with resolution of the pulmonary edema. Over the next several days blood pressure fluctuations between levels of 300/160 and 110/60 were recorded while the patient received parenteral Furosemide and alpramethyl dopa. Several observers noted cyclic fluctuations in alertness with agitation during periods of elevated blood pressure and somnolence during low pressure intervals. Lumbar puncture shortly after admission showed blood tinged CSF under normal pressure with a protein concentration of 280 mgms per l, 7400 RBCs and 10 lymphocytes per mm³. On day two neurologic examination revealed

obtundation and bilateral Babinski responses with absence of papilledema, stiff neck or localizing signs. Several hours later the right pupil reacted less well to light. Ice water stimulation on the left ear canal elicited leftward eye deviation, but right ear stimulation did not cause ipsilateral deviation. A carotid arteriogram with cross compression was interpreted as normal. The following morning both pupils were small and light fixed although the patient appeared more alert and could carry out simple commands. Left ear caloric stimulation response was again normal; however, low amplitude rapid downward eye movements with a slower phase return to the midline were evoked by right ear stimulation and diagnosed as atypical ocular bobbing. Vertebral angiography revealed a large intracerebellar lesion. Craniotomy disclosed a moderate sized hematoma of the vermis with extension into the adjacent right cerebellar hemisphere which compressed the pons and midbrain. The patient never regained consciousness and expired on day 14.

Case 2

A 55 year old, hypertensive, black woman was admitted on September 20, 1972 in deep coma. Headache developed that morning and she had

HYPERTENSIVE CEREBELLAR HEMORRHAGE

LAWRENCE

been examined and sent home from another hospital. She was found unconscious on the floor of her home ten hours later. She was afebrile with a blood pressure of 130/80 mm Hg and a pulse of 80. The right pupil measure 3 mm and left 2 mm. Neither reacted to light or neck pinching. The eyes were in the primary position and did not deviate in response to ice water caloric stimuli to either ear. Papilledema was absent. She was flaccid and hyporeflexic symmetrically. 24 hours later improvement was noted and the patient groaned to painful stimuli. The eye movements horizontally were full except for a left sixth nerve palsy. All four limbs withdrew equally to painful stimuli. Later that day spontaneous ocular bobbing was observed and was increased in frequency by ice water calorics to the left ear. Right ear caloric testing induced tonic conjugate eye deviation to that side. Vertebral angiography showed a large intracerebellar arteriovenous malformation with swelling suggesting a clot. The malformation was partially removed at craniotomy. The patient did poorly post-operatively, with dementia and Parinaud's Syndrome. She died ten months later in a nursing home.

Discussion

Fisher *et al* described the clinical features of acute hypertensive cerebellar hemorrhage in 21 cases and emphasized the difficulty in diagnosis even where clinical suspicion is high.¹ All but two of their patients were over 55. Headache and dizziness were, surprisingly, absent in more than half. Repeated vomiting and the inability to sit, stand or walk unassisted due to truncal ataxia were the most reliable signs. Typically the clinical picture evolved over several hours. On initial examination most patients were drowsy and dysarthric with elevated blood pressures. Nuchal rigidity was

absent in more than half. Hemiparesis or hemiplegia was never observed. Ocular motility abnormalities were frequent, especially inability to fully deviate the eyes to one side or a sixth nerve palsy. Facial weakness of the peripheral variety often accompanied these findings and localized the lesion to the pontomedullary segment. The cerebrospinal fluid was examined in 15 and could not be depended upon to confirm the diagnosis. In 4 it was initially clear, and it was under normal pressure in 7. Repeated puncture was advised to help confirm the diagnosis in these initially negative cases despite the potential risk. The authors recommend immediate angiography or initial craniotomy where suspicion is high. In their series, the appearance of Babinski responses made spontaneous recovery unlikely.

The combination of fluctuating alertness and variable blood pressure suggest the possibility of brain stem compression. Reis and Doba identified a segment of pons in the midline which when compressed or perfused with small amounts of CSF results in elevation of systemic blood pressure in cats.²

Ocular bobbing consisting of downward eye movement with a slower return to the midline in a kind of bobbing motion was described first by Fisher and indicates pontine tegmental impairment.³ Susac *et al* emphasize the need to exclude a compressive lesion of the posterior fossa by angiography or craniotomy whenever horizontal eye movements, either spontaneously occurring or evoked by caloric stimuli, accompany these downward eye movements.⁴ When bobbing occurs in the absence of horizontal eye movements nonremediable destructive pontine tegmental necrosis (usually from hemorrhage or infarction) is found at autopsy.

Radionuclide brain scanning in cerebellar hemorrhage even with the addition of a posterior study is often

disappointingly normal as in our last three cases. The role of computerized transaxial tomography using the EMI Scanner in this entity remains to be defined. One autopsy proven massive primary pontine hemorrhage was definitively outlined by this new technique.

Cerebellar hemorrhage must be excluded in patients with fluctuating blood pressures and unexplained obtundation, particularly where characteristic ocular bobbing occurs with preservation of lateral eye movements. It is to be emphasized that these two signs are often absent and diagnosis still depends upon a high index of clinical suspicion.

Summary

Hypertensive cerebellar hemorrhage must be considered in the differential diagnosis of stroke particularly when obtundation, fluctuating blood pressure, and abnormal eye movements occur.

References

1. FISHER, E. M., FICARD, E. H., POLAK, A., DALAL, P., OJEMANN, R. G.: "Acute Hypertensive Cerebellar Hemorrhage," *J. Neu Ment Dis*, 40, 1965 pp. 38-57.
2. REIS, D. J., DOBA, J.: "Hypertension as a localizing sign of mass lesions of brain stem, (letter), *NEJM*, 287, 26, 1972, pp. 1355-1356.
3. FISHER, C. M.: "Ocular Bobbing," *Arch Neurol*, 11, 1964, pp. 543-546.
4. SUSAC, J. O., HOYT, W. F., DAROFF, R. B., LAWRENCE, W. H.: "Clinical Spectrum of Ocular Bobbing, *J Neurol Neurosurg and Psychiatry*, 33, 1970, pp. 771-775.
5. WELCH, D. M., Seigel, B. A.: "Posterior Fossa Infarction—Results of Brain Scanning," *Radiology*, 110, 2, 1974, pp. 403-407.

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THE VIEW BOX

Prepared by
The Department of Radiology
Washington Hospital Center

A 70 year old black male is admitted with insidious onset of weakness, anorexia and weight loss. There is a mild non-productive cough and pyrexia. The symptoms started approximately 8 weeks ago. A chest radiograph two months prior to admission was normal.

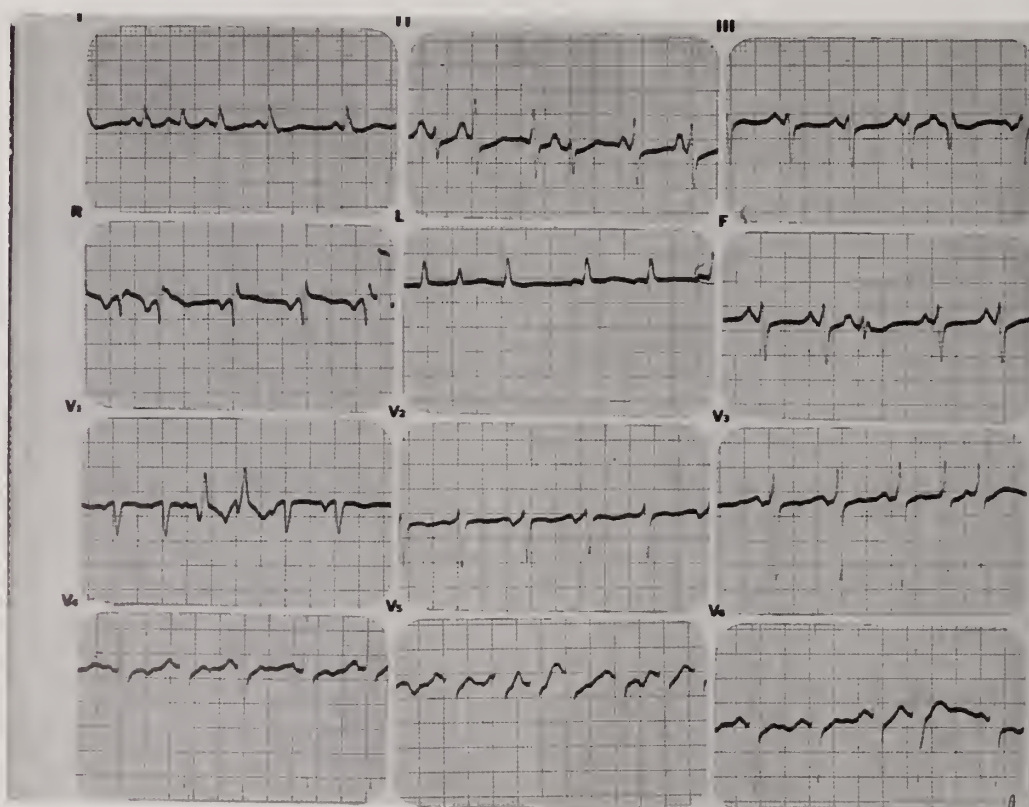
(for diagnosis see page 431)



ECG PROBLEMS

HISTORY: This electrocardiogram was done preoperatively in a 79-year-old white female. Her only cardiac complaints were a sense of palpitation intermittently and slight breathlessness with effort.

(for diagnosis see page 431)



Uhl's Anomaly of the Heart with Atrial Septal Defect and Valvular Pulmonary Stenosis

ROBERT OBMA, M.D., LOWELL W. PERRY, M.D. AND LEWIS P. SCOTT, M.D.

Abstract

The clinical findings, serial catheterizations and angiograms are described in a three and one half year old female with Uhl's anomaly of the right ventricle with associated pulmonary stenosis, patent foramen ovale and hypoplastic left pulmonary artery. Angiographic findings consist of a normally located tricuspid valve ring, a thin-walled, dilated right ventricle, and absent normal right ventricular trabeculations.

Emphasis is placed on the contribution of atrial contraction to forward blood flow through the right ventricle and lesser circulation. Temporary occlusion of the atrial defect with a balloon catheter eliminated right-to-left shunting without significantly diminishing cardiac output or restricting increased cardiac output from exercise. On the basis of these findings surgical closure of the atrial defect will be considered when clinical signs of deterioration develop.

Introduction

In 1952 Uhl described a rare anomaly of the heart in which the right

Our case represents the first of Uhl's anomaly to be reported with associated pulmonary stenosis. Hemodynamic studies performed after surgical correction of the pulmonic stenosis are the first available for Uhl's anomaly associated with significant interatrial septal defect.

ventricular wall is parchment-like due to aplasia or hypoplasia of the myocardial tissue¹. In this anomaly, commonly known as Uhl's anomaly, the right ventricle is dilated, contracts ineffectively and functions principally as a venous reservoir. The right atrium is the primary pumping chamber for systemic venous blood and becomes dilated and hypertrophied^{2,3}. A patent foramen ovale with atrial right-to-left shunting may be present^{4,5}.

Less than 20 cases of Uhl's anomaly appear in the English literature¹⁻¹¹. Of these, only three have been reported with hemodynamic studies. Our case represents the first of Uhl's anomaly to be reported with associated pulmonary stenosis. Hemo-

dynamic studies performed after surgical correction of the pulmonic stenosis are the first available for Uhl's anomaly associated with significant interatrial septal defect.

Case Report

The patient, a baby girl, was first evaluated at seven days of age because of cyanosis and heart murmur noted since birth. The patient was in no distress and there was no clinical evidence of heart failure. The electrocardiogram revealed right ventricular hypertrophy with a qR pattern in the right chest. No Q was present in V6. Chest X-ray showed right ventricular enlargement and normal pulmonary vascularity. Catheterization at seven days of age revealed a 23mmHg gradient across the pulmonary valve (Table I) and a mean gradient of 4mm between the atria with right atrial pressure in excess of left atrial pressure. Cineangiograms revealed moderately severe pulmonary valvular stenosis with a thickened pulmonary valve and post stenotic dilatation of the pulmonary artery (Fig. 1a, b). The left pulmonary artery appeared hypoplastic. Left atrial cineangiogram revealed a left-to-right shunt at the atrial level

UHL'S ANOMALY OF THE HEART

OBMA, PERRY AND SCOTT

TABLE I

Catheterization Data

	Pressure		Oxygen Saturation	
	Age	Age	Age	Age
	7 days	3.5 yrs.	7 days	3.5 yrs.
SVC	—	—	—	73
RA	a 11	11	—	74
	v 6	8		
	m 10	20 (crying)		
RV	37/2*	22/1*	—	74
PA	14/10	19/4	—	74
LA	a 9	10	—	83
	v 6	5	—	
	m 6	14 (crying)		
PV	—	—	—	96
LV	—	105/9	—	83
FA	—	105/55	85	84

* Lowest diastolic pressure recorded.

with an intact ventricular septum and a normally contracting, smooth-walled left ventricle. The great vessels were normally related. The right ventricle, slightly smaller than normal, was distinctly smooth-walled and contracted poorly. The diagnosis at seven days of age was valvular pulmonary stenosis and atrial septal defect. At 18 days of age a Brock pulmonary valvotomy was performed.

Following surgery the patient was lost to follow up until evaluated by our institution at three and one half years of age because of persistent cyanosis. Physical examination revealed a 32 pound little girl in no acute distress with deep central cyanosis, clubbed fingers and toes, normal neck veins, no liver enlargement, normal peripheral pulses and no edema.

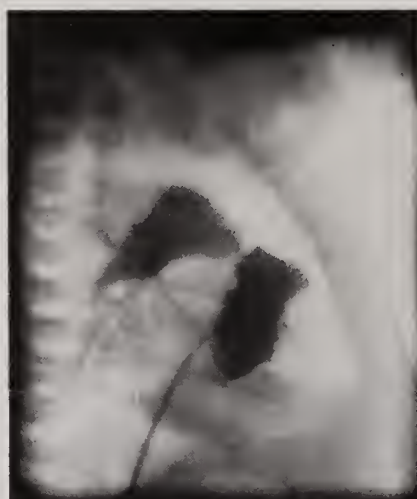


FIG 1 a, b. Right ventricular cineangiogram at seven days of age revealed thickened pulmonary valve and relatively smooth-walled, poorly contracting right ventricle. a. systole b. diastole



Examination of the heart showed the apex to be in the fifth intercostal space in the midclavicular line. There was no murmur. The first heart sound and second sound were of normal loudness; the latter did not close completely with expiration. A third sound was present at the apex. The chest roentgenogram (Figure 2) revealed right ventricular enlargement and normal pulmonary vasculature. The electrocardiogram revealed left ventricular and right atrial hypertrophy. Right ventricular forces were conspicuously absent. (Figure 3)

Cardiac catheterization (Table I) revealed right-to-left shunt at the atrial level and no significant gradient across either semilunar or atrioventricular valve. A 6mmHg transatrial pressure gradient was demonstrated. The right atrial 'a' wave could be clearly demonstrated in both the right ventricular and pulmonary artery pressure tracings. (Figure 4) Right ventricular cineangiograms demonstrated a dilated right ventricle which was smooth-walled and contracted poorly. (Figure 5a, b) The tricuspid valve appeared normally located. There was no tricuspid regurgitation. During late diastole a bolus of blood without contrast material could be seen traversing the tricuspid valve and entering the pulmonary artery with little mixing with apical right ventricular blood. (Figure 5b) The main pulmonary artery was dilated and the left pulmonary artery hypoplastic. The right atrial injection demonstrated a slightly dilated right atrium and atrial right-to-left shunting. Left ventricular cineangiogram revealed a normally contracting, smooth-walled left ventricle and a normally placed aorta.

Intracardiac electrocardiogram revealed simultaneous change in both electrocardiogram and pressure curves as the catheter traversed a normally located tricuspid valve. His bundle



FIG 2. Chest roentgenogram at 3 1/2 years of age. Note apparent right ventricular enlargement and normal pulmonary vascularity.

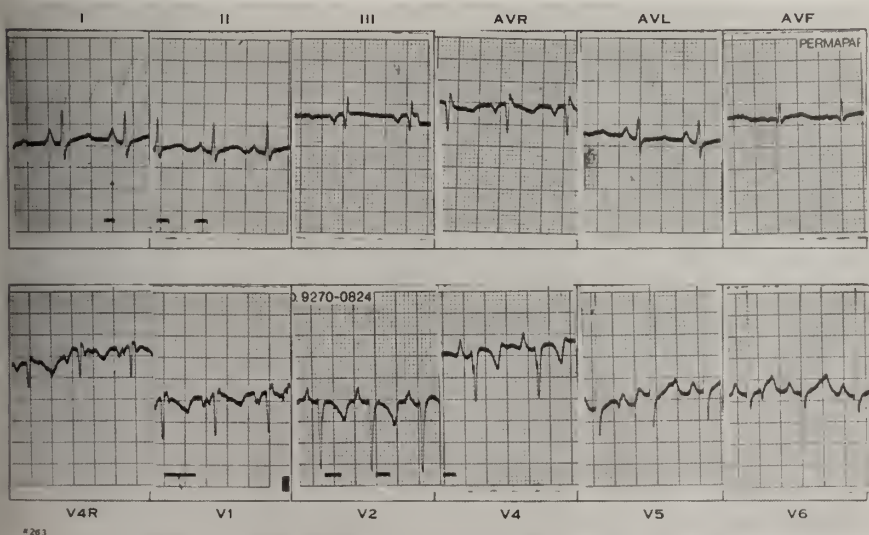
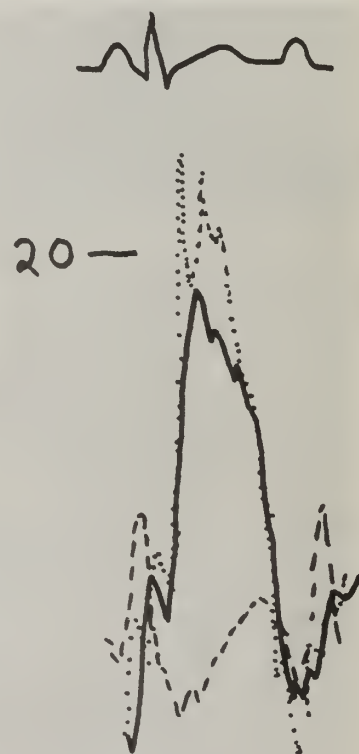


FIG 3. Electrocardiogram at 3 1/2 years of age reveals left ventricular and right atrial hypertrophy. Right ventricular forces are conspicuously absent.



mm Hg ○ —

FIG 4. Right atrial (dashes), right ventricular (dots), pulmonary artery (solid line), pressure tracings superimposed demonstrate clearly the transmission of atrial wave to right ventricle and pulmonary artery.

UHL'S ANOMALY OF THE HEART

OBMA, PERRY AND SCOTT



FIG 5. Right ventricular cineangiogram at 3 1/2 years of age. Smooth walled right ventricle. (a) During systole the right ventricle appears to empty slowly with poor contractions visible in body and outflow tract. (b) In end-diastole, bolus of blood (B) from right atrial kick can be seen in the right ventricle. This bolus could be followed into the pulmonary artery with little mixing with blood at ventricular level.



electrocardiogram was also within normal limits.

Catheters were placed in the superior vena cava and femoral artery and a #8 French Fogarty balloon catheter was advanced to the left atrium. This was inflated with 2.5 cubic centimeters of contrast material and pulled back gradually to occlude the interatrial septal defect. A right atrial angiogram was performed which confirmed almost complete occlusion of the septal defect.

Table II lists the physiological data obtained with partial occlusion of the atrial septal defect and following the administration of isoproterenol to simulate the effect of exercise, and following administration of Oubain to determine the effect of this drug on myocardial function.

The cardiac index decreased insignificantly 15 minutes after partial occlusion of the atrial defect, accompanied by an insignificant increase in 'a' wave and mean venous pressure. Following the administration of 0.02 mg of isoproterenol with the occluded atrial defect, the cardiac output increased without change in central venous pressure. Oubain was administered following deflation of the balloon catheter. Neither cardiac output or central venous pressure changed appreciably. These data indicate that the patient can tolerate temporary occlusion of the atrial defect without significant hemodynamic aberration

and that cardiac output can increase in response to exercise following occlusion of the atrial defect. Failure of significant response to Oubain confirms the absence of myocardial failure and suggests that digitalization will not result in decreased right-to-left shunt or increased cardiac output

Discussion

The clinical and catheterization features of our patient establish the diagnosis of Uhl's anomaly. Our case is unusual because of the presence of pulmonary stenosis and a hypoplastic left pulmonary artery, abnormalities not heretofore associated with the anomaly. The diagnosis might have been suspected in infancy by the presence of angiographic evidence for severe pulmonary stenosis with a paradoxically low peak systolic gradient of 23mmHg across the pulmonary valve and with a peak right ventricular

TABLE II

Physiological Effect of Acute Closure of Atrial Defect with Balloon Catheter and of Administration of Ouabain

	Percent Saturation		Cardiac Index l/min/m ²	Pressure				
	SVC	FA		SVC			FA	
				a,	v,	m	Phasic	Mean
Control	70	86	5.2	8,	6,	5	105/55	78
5 min after								
occlusion of ASD	75	91	5.2	10,	6,	5	100/55	75
15 min after								
occlusion of ASD	74	92	4.4	12,	8,	7	92/60	75
Occlusion plus								
isoproterenol	80	93	6.0	—	—	7	—	110
Control, ASD								
not occluded	73	86	4.6	10,	7,	5	118/62	82
5 min after								
Ouabain .1 mg IV	70	85	5.5	8,	6,	4	108/64	80
30 min after								
Ouabain	70	86	5.2	8,	5,	4	104/57	70

systolic pressure of only 37mmHg. The recognition of the presence of a dilated, relatively smooth-walled and poorly contracting right ventricle without tricuspid regurgitation and with a normally placed tricuspid valve would have supported the diagnosis in infancy.

Common hemodynamic findings reported in cases of Uhl's anomaly include 1) a prominent atrial 'a' wave with transmission of the 'a' wave impulse to the right ventricular and pulmonary arterial pressure tracings, and 2) low peak systolic pressures in the right ventricle and pulmonary artery. Atrial right-to-left shunt has been present in cases with associated patent foramen ovale^{4,5,11}.

The angiographic findings in Uhl's anomaly are 1) a normally located tricuspid ring, 2) a thin walled, markedly dilated right ventricle, and 3) absence of normal right ventricular trabeculation^{2,3}. To these we add a) decreased right ventricular wall movement with most of systolic inward motion at the base of the heart, b) a clearly visible "atrial kick" in the ventricle, c) a visible forward negative washout of blood through the tricuspid valve and right ventricular outflow tract, partially bypassing the reservoir of blood at the right ventricular apex, and d) a moderately dilated, vigorously contracting right atrium.

Uhl's anomaly can be distinguished from Ebstein's malformation by the demonstration of normal location of the tricuspid valve and annulus. Hypoplastic right ventricle is excluded by the presence of a dilated rather than diminutive right ventricle.

Clinical findings common to cases without pulmonary stenosis include cyanosis with no significant heart murmur, diminished right ventricular forces on electrocardiography, normal or increased pulmonary vascularity and right ventricular dilatation on chest roentgenograms without palp-

able right ventricular precordial activity. The ejection murmur noted at the base of the heart at age seven days in our case was not present in any of the cases of isolated Uhl's anomaly without pulmonary stenosis.

The majority of reported cases of severe Uhl's anomaly have died of intractable right heart failure in infancy or childhood. One patient with associated atrial defect lived 47 years, dying of a cerebral hemorrhage⁴, and two cases with a mild degree of the malformation died at ages 57 and 84^{7,9}.

Of prime importance in the present case is the possibility of surgical therapy for the patent foramen ovale. Acute occlusion of the defect at time of catheterization suggests this would be tolerated. Enthusiasm for closure of the atrial defect is tempered in the present case by lack of knowledge of the effect of the surgical incision on the pumping action of the right atrium in this lesion and by knowledge of the disastrous consequences of closure of the atrial defect in individuals with Ebstein's malformation. The only survival to adult life in the patient with a severe enough degree of the malformation to cause cardiomegaly was in the case associated with an atrial septal defect.

In the present case palliation with a superior vena cava to right pulmonary artery anastomosis would seem unwise because of hypoplasia of the left pulmonary artery, and, indeed, such a procedure has been uniformly fatal^{3,7,10}. A systemic-pulmonary arterial shunt would probably lead to more rapid than usual deterioration because of the hypoplastic right ventricle. In the case in which a Pott's anastomosis was performed, the patient died one month post-operatively.⁸ Atrial septostomy in conjunction with a Waterston shunting procedure has been performed with two fatalities in the two cases at-

tempted¹⁰. Because of the poor results with various surgical procedures we have elected not to treat the patient at this time. She is now growing well and not disabled. Should clinical deterioration occur, closure of the atrial septal defect or procedures aimed at increasing pulmonary blood flow will be considered.

References

1. UHL, H. S.: Previously undescribed congenital malformation of the heart: almost total absence of the myocardium of the right ventricle. *Bulletin Johns Hopkins Hosp.* 91:197-205, 1952.
2. ARCILLA, R. A., GASUL, B. M.: Congenital aplasia or marked hypoplasia of myocardium of right ventricle (Uhl's anomaly). *J. Pediat.* 58: 381-388, 1961.
3. ZUBERBUHLER, J. R., BLANK, E.: Hypoplasia of right ventricular myocardium. *Amer. J. Roentgenology.* 110:491-496, 1970.
4. REEVE, R., MACDONALD, D.: Partial absence of right ventricular myocardium: partial parchment heart. *Amer. J. Cardiol.* 19:415-419, 1964.
5. Case records of the Massachusetts General Hospital (Case 38201). *New Eng. J. Med.* 246:785-790, 1952.
6. CUMMING, G. R., BOWMAN, J. M., WHYTHEAD, L.: Congenital aplasia of myocardium of right ventricle (Uhl's anomaly). *Amer. Heart Jour.* 70:671-676, 1965.
7. GOULD, L., GUTTMAN, B., CARASCO, J., LYON, A. F.: Absence of right ventricular musculature. *Amer. Jour. Med.* 42:636-641, 1967.
8. PERRIN, E. U., MEHRIZI, A.: Isolated free-wall hypoplasia of the right ventricle. *Amer. Jour. Dis. Child.* 109: 55, 1965.
9. SEGIURA, M., HAYASHI, T., UENO, K.: Partial absence of the right ventricular muscle in the aged. *Jap. Heart Jour.* 11:582-585, 1970.
10. KINARE, S. G., PANDAY, S. R., DESHMUKH, S. M.: Congenital aplasia of the right ventricular myocardium (Uhl's anomaly). *Dis. Chest* 55:429-431, 1969.

UHL'S ANOMALY OF THE HEART

OBMA, PERRY AND SCOTT

-
11. ACKNER, M. A., ROBINSON, M. J., JAMISON, W. L., LEWIS, D. H.: Isolated right ventricular hypoplasia with atrial septal defect or patent foramen ovale. *Circulation*. 24:1388-1402, 1961.
 12. RASHKIND, W. J., Atrial septostomy in congenital heart disease. *Advances in Ped. Year Book Publishers, Inc.*, Chicago, 1969. Vol. 16, 228.

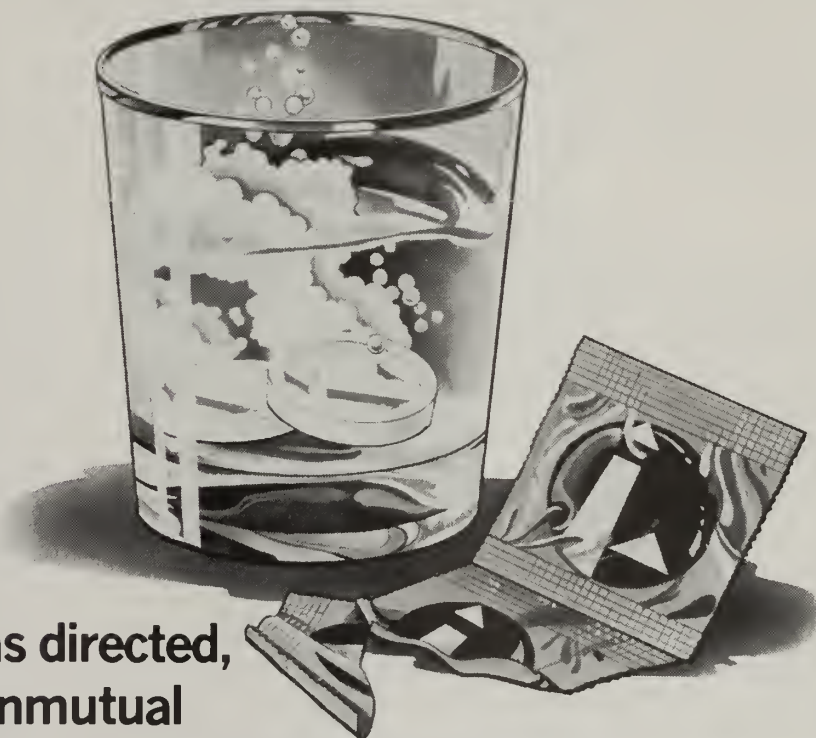
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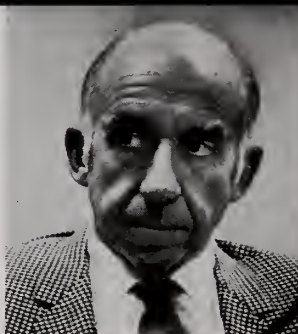
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"In the total picture of dealing with health problems in this country there is a potential for detail men to play a meaningful role."

The Positive Influence

My contact with representatives and salesmen of the pharmaceutical industry is the type of contact that people in a medical center, research people, and academic people have and that's in all likelihood on a somewhat different level from that of the practicing physician.

Let me touch on how I personally perceive the role of the sales representative. These men reach large numbers of health professionals. Thus they could be—and at times actually are—disseminators of useful information. They could consistently serve a real educational function in their ability to discuss their products.

At present they do distribute printed material, brochures and pamphlets—some of it scientifically sound and therefore truly useful—as well as some excellent films produced by the pharmaceutical industry. When they function in this

Opinion
&
Dialogue

He a Source of Information?

Yes, with certain reservations. The average sales representative has a great fund of information about the drug products he is responsible for. He is usually able to answer most questions fully and intelligently. He can also supply reprints of articles that contain a great deal of information. Here, too, I exercise some caution. I usually accept most of the statements and opinions that I find in the papers and studies which come from the larger teaching facilities. I go without saying that a physician should also rely on other sources for his information on pharmacology.

Training of Sales Representatives

Ideally, a candidate for the position as a sales representative of a pharmaceutical company should be a graduate pharmacist who has a questioning mind. I don't think this is possible in every case, and so it becomes the responsibility

of the pharmaceutical company to train these individuals comprehensively. It is of very great importance that the detail man's knowledge of the product he represents be constantly reviewed as well as updated. This phase of the sales representative's education should be a major responsibility of the medical department of the pharmaceutical company.

I am certain that most of these companies take special care to give their detail men a great deal of information about the products they produce—information about indications, contraindications, side effects and precautions. Yet, although most of the detail men are well informed, some, unfortunately, are not. It might be helpful if sales representatives were reassessed every few years to determine whether or not they are able to fulfill their important function. Incidentally, I feel the same way about periodic assessments of everyone

in the health care field, whether they be general practitioners, surgeons or salesmen.

Value of Sampling

I personally am in favor of limited sampling. I do not use sampling in order to perform clinical testing of a drug. I feel that drug testing should rightly be left to the pharmacology researcher and to the large teaching institutions where such testing can be done in a controlled environment.

I do not use samples as a "starter dose" for my patients. I do, however, find samples of drugs to be of value in that they permit me to see what the particular medication looks like. I get to see the various forms of the particular medication at first hand, and if it is in a liquid form I take the time to taste it. In that way I am able to give my patients more complete information about the particular medications that I prescribe for them.

capacity they are indeed useful; particularly in the fact that they disseminate broadly based educational material and serve not just as "pushers" of their drugs.

The Other Side of the Coin

Obviously, the pharmaceutical companies are not producing all this material as a labor of love—they are in the business of selling products for profit. In this regard the ambitious and improperly motivated sales representative can exert a negative influence on the practicing physician, both by presenting a one-sided picture of his product, and by encouraging the practitioner to depend too heavily on drugs for his total therapy. In these ways, the salesman has often distorted objective reality and undermined his potential role as an educator.

The Industry Responsibility

Since the detail man must be an information resource as well as a representative of his particular pharmaceutical company, he should be carefully selected and

thoroughly trained. That training, perforce, must be an ongoing one. There must be a continuing battle within and with the pharmaceutical industry for high quality not only in the selection and training of its sales representatives, but also in the development of all of its promotional and educational material.

The industry must be ready to accept constructive as well as corrective criticism from experts in the field and consumer spokesmen, and be willing to accept independent peer review. The better educated and prepared the salesman is, the more medically accurate his materials, the better off the pharmaceutical industry, health professionals and the public—*i.e.*, the patients—will be.

Physician Responsibility

The practicing physician is in constant need of up-dated information on therapeutics, including drugs. He should and does make use of drug information and answers to specific questions supplied by the pharmaceutical representative. However, that informa-

tion must not be his main source of continuing education. The practitioner must keep up with what is current by making use of scientific journals, refresher courses, and information received at scientific meetings.

The practicing physician not only has the right, but has the responsibility to demand that the pharmaceutical company and its representatives supply a high level of valid and useful information. I feel certain that if such a high level is demanded by the physician as well as the public, this demand will be met by an alert and concerned pharmaceutical industry.

From my experience, my impression is that sectors of the pharmaceutical industry are indeed ethical. I challenge the industry as a whole to live up to that word in its finest sense.

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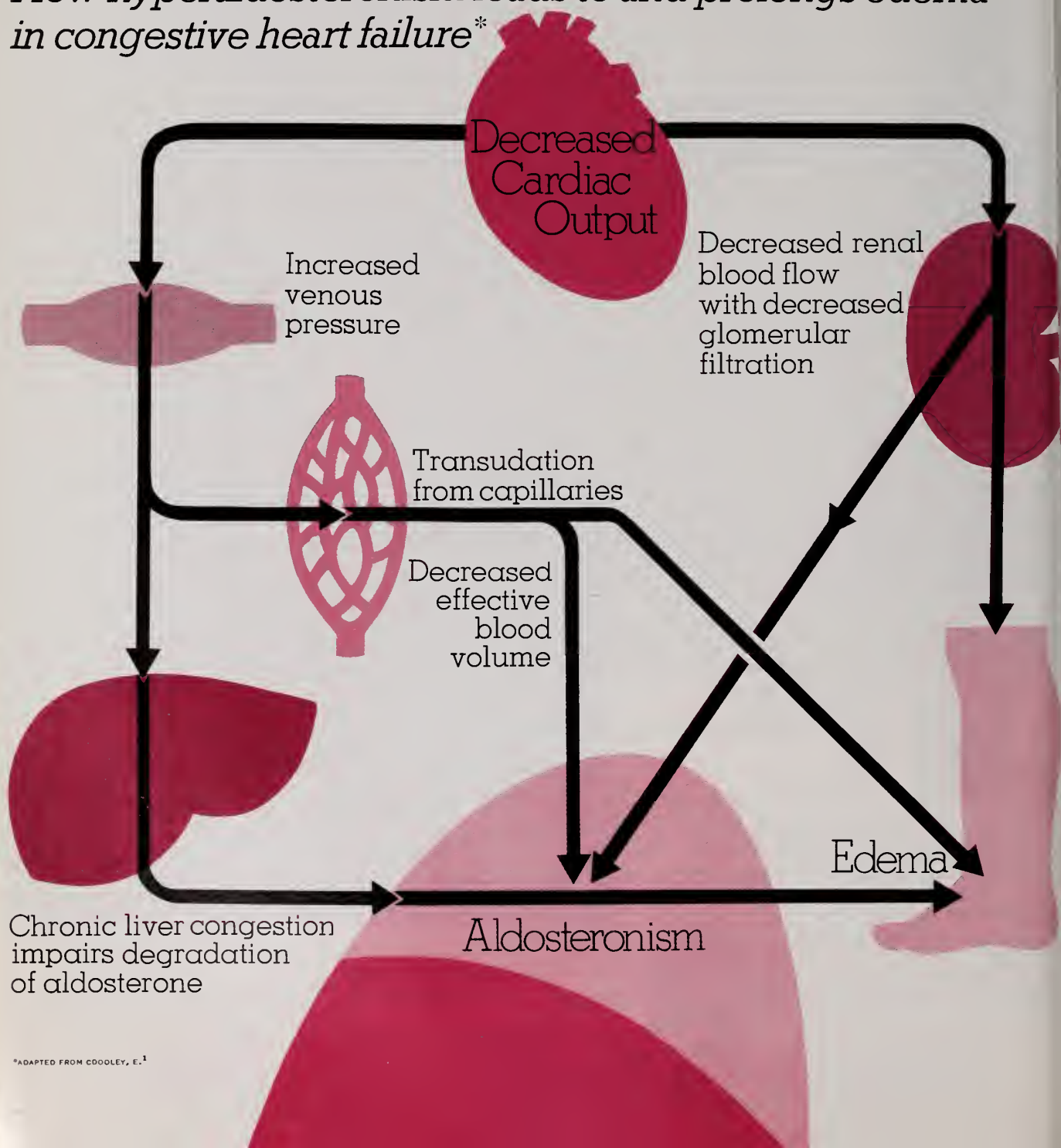
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 - Avoids acute volume depletion and aldosterone rebound.²
3. As a daily diuretic in combination with a daily dose of a thiazide
 - Permits daily additive diuretic effect while maintaining potassium balance.

Indications—Essential hypertension; edema or ascites of congestive heart failure, cirrhosis of the liver and the nephrotic syndrome; idiopathic edema. Same patients with malignant effusions may benefit from Aldactone (spironolactone), particularly when given with a thiazide diuretic.

Contraindications—Acute renal insufficiency, rapidly progressing impairment of renal function, anuria and hyperkalemia.

Warnings—Potassium supplementation may cause hyperkalemia and is not indicated unless a glucocorticoid is also given. Discontinue potassium supplementation if hyperkalemia develops. **Usage of any drug in women of childbearing age requires that the potential benefits of the drug be weighed against its possible hazards to the mother and fetus.**

Precautions—Patients should be checked carefully since electrolyte imbalance may occur. Although usually insignificant, hyperkalemia may be serious when renal impairment exists; deaths have occurred. Hyponatremia, manifested by dryness of the mouth, thirst, lethargy and drowsiness, together with a low serum sodium may be caused or aggravated, especially when Aldactone is combined with other diuretics. Elevation of BUN may occur, especially when pretreatment hyperazotemia exists. Mild acidosis may occur. Reduce the dosage of other antihypertensive drugs, particularly the ganglionic blocking agents, by at least 50 percent when adding Aldactone since it may potentiate their action.

Adverse Reactions—Drowsiness, lethargy, headache, diarrhea and other gastrointestinal symptoms, maculopapular or erythematous cutaneous eruptions, urticaria, mental confusion, drug fever, ataxia, gynecomastia, inability to achieve or maintain erection, mild androgenic effects, including hirsutism, irregular menses and deepening voice. Adverse reactions are infrequent and usually reversible.

Dosage and Administration—For essential hypertension in adults the daily dosage is 50 to 100 mg. in divided doses. Aldactone may be combined with a thiazide diuretic if necessary. Continue treatment for two weeks or longer since an adequate response may not occur sooner. Adjust subsequent dosage according to response of patient.

For edema, ascites or effusions in adults initial daily dosage is 100 mg. in divided doses. Continue medication for at least five days to determine diuretic response; add a thiazide or organic mercurial if adequate diuretic response has not occurred. Aldactone dosage should not be changed when other therapy is added. A daily dosage of Aldactone considerably greater than 75 mg. may be given if necessary.

A glucocorticoid, such as 15 to 20 mg. of prednisone daily, may be desirable for patients with extremely resistant edema which does not respond adequately to Aldactone and a conventional diuretic. Observe the usual precautions applicable to glucocorticoid therapy; supplemental potassium will usually be necessary. Such patients frequently have an associated hyponatremia—restriction of fluid intake to 1 liter per day or administration of mannitol or urea may be necessary (these measures are contraindicated in patients with uremia or severely impaired renal function). Mannitol is contraindicated in patients with congestive heart failure, and urea is contraindicated with a history or signs of hepatic coma unless the patient is receiving antibiotics orally to "sterilize" the gastrointestinal tract.

Glucocorticoids should probably be given first to patients with nephrosis since Aldactone, although useful for diuresis, will not directly affect the basic pathologic process.

For children the daily dosage should provide 1.5 mg. of Aldactone per pound of body weight.

References: 1. Coodley, E.: Consultant 12:106-107, 109, 111, 113, 115 (July) 1972. 2. Thorn, G. W., and Louler, D. P.: Am. J. Med. 53:673-684 (Nov.) 1972.

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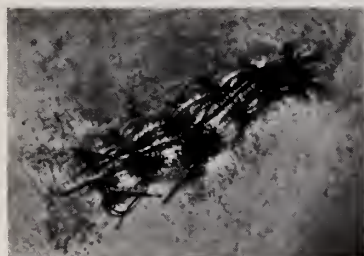
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POST GRADUATE EDUCATION

When To Consider Coronary Artery Bypass Surgery

The ability to bypass a stenotic or occluded coronary artery by an aortocoronary autogenous saphenous vein graft, or by internal mammary artery to coronary artery anastomosis, is an established technical fact. The precise role of this procedure in the overall management of coronary heart disease is not yet so well defined. An understanding of what such surgery can and cannot accomplish is necessary before establishing indications and contraindications. Unfortunately, insufficient time and clinical investigation have permitted many questions to remain still unanswered. Nevertheless, the physician is faced with making decisions today within the limits of today's knowledge.

Coronary bypass can bring physiologic flows of blood to myocardium inadequately supplied by a proximal occluding lesion. The vein bypass can remain patent for at least a year about 65-75% of the time and indications are that the patency rate over the next two years will be reduced by only another 5-6%. Significant relief of angina can be obtained in approximately 85% of patients. Reversal of segmental ventricular dysfunction may be accomplished in certain instances where it is based on ischemia rather than on fibrosis. Coronary bypass cannot retard or reverse the underlying atherosclerotic process and cannot reverse ventricular dysfunction based on myocardial scarring. Therefore, prevention of future myocardial infarction and prolongation of life may not be achieved by such surgery, although this remains to be proven. Fundamental to the candidacy of any patient for bypass surgery is the presence of at least 70% occlusion of a major coronary vessel with an adequately sized and sufficient disease free distal runoff, in the presence of good overall ventricular function. This must be determined by selective coronary arteriography and left ventriculography. In the light of these facts, the following stratification of indications for coronary bypass surgery is presented:

Definite Indications:

Stable angina of disabling degree despite maximum medical management (including Propranolol) is probably the most clear cut indication for recommending bypass surgery. The amount of angina considered disabling is, of course, highly

individualized according to the patient's age, outlook, life style, and so on. In general, when the symptom has prompted an alteration of the patient's life style in a manner unacceptable to him, it is time to consider bypass surgery. The patient with recurrent coronary insufficiency (prolonged pain not responding to nitroglycerine), requiring frequent hospitalizations, can be considered electively in the same manner as the patient with disabling stable angina. The patient with stable angina, normal ventricular function, and favorable coronary anatomy faces a less than 6% (maybe as low as 2%) hospital mortality in most large centers. He also faces a 7-20% chance of sustaining a myocardial infarction intra or post operatively. Nevertheless, his chances of symptomatic relief and improved quality of life are excellent, although the duration of relief is as yet uncertain.

Probable Indications:

Unstable angina, only when persistent or recurrent after hospitalization despite maximum medical management, and especially when associated with recurrent ventricular dysrhythmia and/or localized electrocardiographic injury current during pain, may be considered a semi-emergency indication for bypass surgery. This group represents a subset of the general category of unstable angina and operation is proposed for the control of symptoms. Its effect on preventing myocardial infarction or prolonging life is not yet established.

Unstable angina includes various syndromes such as initial angina, progressive (or "crescendo") angina, and angina decubitus. These may all be considered pre-infarction syndromes. The data in the literature is unclear, not only on the surgical outcome but on the non-operative prognosis. The more persistent and prolonged the symptoms and the more impending the infarction, then probably the greater the indication for surgery. The surgical mortality has generally been higher than that in stable angina, but not prohibitive, and the relief of symptoms has been comparable. The best time to proceed with operation, and the long term results compared to medical therapy, have yet to be elucidated by studies now in progress.

POST GRADUATE EDUCATION

Possible Indications:

Information is beginning to become available on the prognosis for patients with angina based on the location and extent of their disease as defined by coronary arteriography. It is possible, therefore, that a patient with stable angina of non-disabling degree who has significant main left coronary narrowing or significant narrowing of the proximal portions of all three major coronary arteries (or perhaps a severe (90%+) narrowing of the proximal left anterior descending with significant disease in the arteries supplying the major collaterals), could be considered a candidate for surgery. Such anatomic change might be suspected when graded exercise testing produces ST segment depression of greater than two millimeters. Some information is available concerning the relatively adverse outlook for these patients without surgery, and preliminary data supports the hope that surgery may improve their prognosis. However, the completion of a confirming randomized, controlled trial is still pending. Other possible indications based on scattered reports of success are the myocardial infarction occurring in the hospital post coronary arteriography, if surgery can be performed within four hours of onset; the myocardial infarction with cardiogenic shock which

can be supported only by a cardiac assist device (such as balloon pumping); and the patient with recurring life threatening ventricular tachycardia or fibrillation and a localized area of ventricular dysfunction.

Non-indications:

At present the following clinical settings are not considered indications for coronary bypass except perhaps on an experimental basis: acute myocardial infarction, severe diffuse myocardial dysfunction, or the asymptomatic or postmyocardial infarction patient for "prophylactic" operation.

Summary and Conclusion:

In as much as data do not yet exist to prove that coronary bypass surgery prevents myocardial infarction or prolongs life, such surgery should be considered primarily for the relief of symptoms. The above recommendations are necessarily tentative and subject to continuous modifications and updating as more information becomes available.

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THE VIEW BOX

(from page 411)

DIAGNOSIS: MILIARY TUBERCULOSIS

Note the myriad of tiny (2 to 3 mm.) discrete nodules in the interstitium of both lungs. There is even distribution throughout both lungs and there is no hilar lymph adenopathy or pleural effusion.

The radiographic differential diagnosis of this miliary pattern (granulomatous pneumonitis) includes fungus infection, sarcoidosis, eosinophilic granuloma and occupational diseases secondary to inhalation such as silicosis, in addition to miliary tuberculosis. The rapid occurrence of this pattern in an elderly black patient with pyrexia should suggest the diagnosis.

***Edited by Gunter J. Augustin, M.D.
Senior Attending Radiologist, Washington
Hospital Center, Washington, D.C.***

ECG PROBLEMS

(from page 412)

INTERPRETATION: 1. Frequent supraventricular premature beats, some with aberrant conduction.
2. ST-T changes consistent with myocardial ischemia.
3. Borderline left axis shift.

This tracing shows many premature beats, all of which are supraventricular. Although most of the QRS complexes in these ectopic beats are similar to those in the sinus beats, a few are different and might suggest ventricular premature beats. The third beat in lead AVF and the third and fourth complexes in V_1 are particularly abnormal. The QRS complexes are prolonged, the QRS contours are different from those of the other beats in the same leads, and the ST-T contours are grossly different. All these are attributes of ventricular premature beats. However, preceding each of these beats is a discernible atrial complex. In AVF, the ST-T complexes of the second beat are distorted by an upward deflection which represents the P wave of this atrial premature beat. The same can be said of the ST-T contours of the second complex in V_1 . Between the two abnormal complexes in V_1 there is a sharp, inverted wave which could be the apex of the T wave, but probably represents a superimposed P wave. The QRS complexes in these three beats are abnormal because of their prematurity. The ventricular repolarization following the preceding beat has not yet been completed. This forces the ventricles to depolarize along somewhat abnormal (aberrant) pathways. It is characteristic that the aberrant complex will resemble the QRS of right bundle branch block in lead V_1 , although this is not necessarily the case. The fourth beat in V_1 merits a little special consideration. The apparent inverted P wave following the third beat (the first atrial premature beat in that lead) may well represent retrograde depolarization of the atria by that ectopic beat. The fourth beat (the second premature beat) probably represents depolarization of the ventricles as a result of that retrograde atrial depolarization. This sequence constitutes an echo beat. In this situation the first premature beat activates the A-V junction which in turn activates the atria in a retrograde manner and the ventricles once again in the antegrade, aberrant, manner.

Edited by Robert R. Montgomery, M.D.

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MANUSCRIPT

The entire manuscript, including footnotes and case reports, should be submitted unrolled, with double type spacing. An original copy and one carbon copy should be submitted, and a carbon copy should be retained by the author.

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The by-line, the author's given name and initial or given name alone should be supplied. The M.D. degree or highest academic degree should be listed for each author. Not more than six names should be included as authors, unless the communication is the report of a committee.

The footnotes, hospital and university affiliation when study was done, should be listed. Present affiliation and location (if different from that at time of study) should be given. Acknowledgements should be limited to persons, foundations, agencies or companies supplying drugs, funds or apparatus free of charge or otherwise making an extensive contribution to the study.

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The number of references should not exceed 18 single complete bibliographic citations, except in Special Articles.

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Lyons, W.S., Peabody, J.W.: Com-
plications of Cardiac Pacemakers,
Medical Annals of D.C., 1973, 42,
165.

TEXT

Use generic or descriptive names of drugs when available. Trade names, capitalized, may be given in parentheses when the drug is first mentioned.

Statistics should be checked for consistency within the text and for agreement with graphs or tables.

Laboratory data should not be given in abbreviated form but in full (e.g., "hemoglobin level, 12 Gm. per 100 ml." rather than "Hb. 12 GM.%).

Figures should be used for number 10 and above, laboratory measurements, percentages, and ages.

Metric equivalents should be given for dosage and body height and weight.

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Abbreviations should be used sparingly, with expansion given for those not listed in standard medical dictionaries.

The meaning of "we" should be clarified, especially if there is only one author. Avoid use of editorial "we."

SUBHEADINGS

One center heading should be supplied for about every three pages of double-spaced text copy. Subdivisions of main topics should be indicated by side headings.

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The summary should be brief, giving specific facts concerning the study and its results.

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The street address of one author should be given at the end of the article for reprint requests and correspondence.

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The title should be given at top of the page for each table.

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The meaning of abbreviations should be clear, with those not listed in standard medical dictionaries expanded in a footnote to the table.

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Only necessary illustrations should be submitted.

Photographs should be submitted as unmounted black-and-white glossy prints.

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Lettering on a figure should be checked for correct spelling and style consistent with the manuscript.

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**HYPERTENSION DETECTION IN
EXISTING OUTPATIENT CLINICS
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**TORSION OF THE TESTIS AND
ITS APPENDAGES**

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Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive dis-

orders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anti-convulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful

OCT 30 1974

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According to her major symptoms, she is a psychoneurotic patient with severe anxiety. But according to the description she gives of her feelings, part of the problem may sound like depression. This is because her problem, although primarily one of excessive anxiety, is often accompanied by depressive symptomatology. Valium (diazepam) can provide relief for both—as the excessive anxiety is relieved, the depressive symptoms associated with it are also often relieved.

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two, although it may take longer in some patients. In addition, Valium (diazepam) is generally well tolerated; as with most CNS-acting agents, caution patients against hazardous occupations requiring complete mental alertness.

Also, because the psychoneurotic patient's symptoms are often intensified at bedtime, Valium can offer an additional benefit. An *h.s.* dose added to the *b.i.d.* or *t.i.d.* treatment regimen can relieve the excessive anxiety and associated depressive symptoms and thus encourage a more restful night's sleep.

For further information on this subject, the following references are provided:

1. Henry BW, *et al*: *Dis Nerv Syst* 30:675-679, Oct 1969.
2. Hollister LE, *et al*: *Arch Gen Psychiatry* 24:273-278, Mar 1971.
3. Claghorn J: *Psychosomatics* 11:438-441, Sept-Oct 1970.

surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of child-bearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies.

Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle



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CONTENTS

**SCIENTIFIC
ARTICLES**

Hypertension Detection in Existing Outpatient Clinics of Metropolitan Washington, D.C. William J. Mroczek, M.D., Margene Wilson, R.N. and Frank A. Finnerty, Jr., M.D.	437
Torsion of the Testis and Its Appendages. Glenn W. Geelhoed, M.D.	441
Bilateral Successive Adrenal Pheochromocytoma With Complicating Essential Hypertension. Noel M. Doromal, M.D. and Philip Middleton, M.D.	451
Isolated Agenesis of The Right Pulmonary Artery Terminating in Pneumonia in a Young Adult. W. V. R. Vieweg, CDR, R. S. Conte, LCDR and R. F. Schillaci, CDR	457

**SPECIAL
ARTICLE**

HMO—Friend or Foe? Horace W. Bernton, M.D.	445
--	-----

**OTHER
FEATURES**

Scientific Editorial	5
Evaluation of Penicillin Hypersensitivity. Halla Brown, M.D. and revised by Solomon Barr, M.D., Richard Nicklas, M.D., and Isaac Weiszer, M.D.	444
The View Box	485
Edited by Gunter J. Augustin, M.D.	
Book Reviews	
Before Addiction: How to Help Youth. (Lieberman, Caroff and Gottesfeld) Reviewed by John G. Stubenbord, M.D.	
Corneal Graft Failure. (Ciba Foundation Symposium) Reviewed by Michael A. Lemp, M.D.	
Information for Authors	488
Advertising and Subscription Information	490
Index to Advertisers	490

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SCIENTIFIC Editorial

EVALUATION OF PENICILLIN HYPERSENSITIVITY

Penicillin is the most frequent cause of anaphylaxis, which occurs in 10-40 out of 100,000 injections, and results in about 600 fatalities per year. More distressing is the fact that in 3/4 of these reactions, the patient knows that he is allergic to penicillin and is not asked by the physician, or in fact tells the physician but is still given penicillin.

The immunology of penicillin sensitivity is now well enough understood so that the reaction of a patient thought to be sensitive after a careful history can be predicted with at least 95% accuracy after skin testing.

Penicillin is a small molecule. 95% is degraded to form a benzyl-penicilloyl (BPO) hapten; BPO therefore is termed the "major" antigenic determinant. It is responsible for accelerated and late urticarial reactions. The minor determinants comprise small amounts of at least 5 other antigens: benzyl penicillin, benzyl penicilloate, benzyl penilloate, alpha benzyl penicilloyl amine, and benzyl penicilloic acid. These minor determinants cause immediate reactions (anaphylaxis and urticaria) as well as the late syndrome of recurrent urticaria and arthralgia.

Types of Penicillin Reactions

Type	Onset After Administration	Reactions
A. Immediate	Less than 2 hours	Anaphylaxis Urticaria
B. Accelerated	2-48 hours	Urticaria Laryngeal edema
C. Late Urticarial	Less than 2 days	
D. Recurrent urticaria and arthralgias	2-21 days	
E. Late exanthems	Variable	

Penicillin elicits the formation of antibodies of classes IgM, IgG, and IgE. The last, also known as reagenic antibody, is the mediator of immediate, accelerated, and late urticarial reactions. Almost all persons, even those without a history of penicillin administration, have been found to have IgM antibodies to penicillin in their serum. Immunization may have occurred from drinking milk, eating meat,

or from other sources in the environment which may contain penicillin. The titer of IgM antibodies may also be elevated in patients developing late exanthems during penicillin therapy. IgG antibodies usually develop 5-10 days after penicillin therapy. They may compete for receptor sites on mast cells with IgE antibodies, thereby acting as "blocking" antibodies which could theoretically prevent anaphylactic reactions and cause urticaria to subside. Certainly the presence of anti-penicillin antibodies other than IgE antibodies does not necessarily imply clinical sensitivity to penicillin.

It should be emphasized that a careful history is the most important clue to penicillin hypersensitivity. In a patient giving an unequivocal history of penicillin allergy, substitution of another antibiotic is preferable, since even a prick test can result in anaphylaxis. Skin testing should be done only if penicillin is mandatory for the patient's therapy.

The incidence of positive skin tests decreases with time from the last administration of penicillin. By the same token, skin tests are negative right after a penicillin reaction while the highest degree of reactivity occurs two weeks later. Since a penicillin skin test with whole antigen may sensitize a patient, testing is performed with BPO hapten attached to a molecule of polylysine (PLL), which is not sensitizing. During the 24 hours preceding skin testing, the patient should avoid antihistamines and/or epinephrine since these may decrease skin reactivity. As a precautionary measure, a tourniquet should be placed under the arm, and epinephrine should be drawn into a syringe.

Unfortunately at present, the major and minor determinants, other than Benzyl penicillin, are not commercially available, although efforts are being made to achieve this. At the present time, unless the physician has access to both major and minor determinants, it is safer to refer the patient to an allergist who does.

Negative immediate skin tests to both major and minor determinants virtually exclude the possibility of an anaphylactic reaction and reduce the probability of an accelerated urticarial reaction. On the other hand, a positive skin test to Penicillin G or the other minor determinants is associated with a

very high probability of immediate or accelerated reactions to penicillin.

In regard to penicillin derivatives, semisynthetic penicillins and cephalosporin C derivatives have been developed by modification of the side chain. Since the 6 amino penicillanic acid nucleus is responsible for most antigenic activity, oxacillin, nafcillin, ampicillin, and carbenicillin may produce the same types of allergic reaction as Penicillin G. Ampicillin, in addition to producing true hypersensitivity reactions, does produce a high incidence of erythematous eruptions, probably unrelated to penicillin allergy. These often occur after 1-3 weeks of therapy and more frequently associated with other disease entities such as infectious mononucleosis, where it occurs in close to 100% of the cases.

If a patient who is sensitive to penicillin develops enterococcal bacterial endocarditis where the administration would be life saving, desensitization may have to be attempted. While proceeding, every precaution should be made to avoid anaphylaxis, and the concomitant use of antihistamines and steroids is usually necessary. Should this situation arise, schedules for desensitization can be found in most textbooks of allergy.

The immunology of other antibiotics is poorly understood. Since most of these drugs are not isotonic, and the antigens have not been elucidated, the physician can perform only scratch tests and saline controls. In vitro procedures such as MIF and lymphocyte transformations have been shown to be

of little value mainly because of their lack of consistency.

In summary, there is no doubt allergic reactions to penicillin represent a significant medical problem in the country. It is also clear, however, that penicillin is the only antibiotic where extensive studies have finally provided us with a means of determining hypersensitivity.

HALLA BROWN, M.D.

Revised by

SOLOMON BARR, M.D.

RICHARD NICKLAS, M.D.

ISAAC WEISZER, M.D.

Editor's Note: We are not only grateful to Dr. Brown, who prepared this at our request, but to Drs. Barr, Nicklas and Weiszer who were kind enough to revise this into final form when Dr. Brown's illness made it impossible for her to do so.

References

1. LEVINE, B. B. & Zolov, D. M.: Prediction of penicillin allergy by immunological tests. *J. Allergy* 43:231-244, 1969.
2. In MIESCHER AND MUELLER-EBERHARD IMMUNOPATHOLOGY, chapter on drug reactions by B. B. Levine.
3. PATTERSON, ROY: *Allergic Diseases*, published by J. B. Lippincott Co., Philadelphia, Pennsylvania 1972.
4. BORMAN, C. W. & VANARSDEL, P. O. JR.: Penicillin allergy in children: The role of immunology tests in its diagnosis. *J. Allergy* 43:267-272, 1969.



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SCIENTIFIC ARTICLES

Hypertension Detection in Existing Outpatient Clinics of Metropolitan Washington, D.C.

WILLIAM J. MROCZEK, M.D., MARGENE WILSON, R.N. AND FRANK A. FINNERTY, JR., M.D.

Abstract

Blood pressures were determined in the outpatient clinics of three Washington D.C. area hospitals covering a broad range of clinical practice. Blood pressures were measured in 1247 patients by specially trained high school students under the direction of a nurse. Fifty-one percent of the patients screened had elevated blood pressures and after two verification blood pressures 84% of these patients had documented sustained hypertension. Review of hospital records showed that 426 of the 637 patients with elevated blood pressures had been seen in an internal medicine clinic within the past year; however, only 155 of these patients had a blood pressure recorded in the chart during the past year. A review of 4461 clinic visits in 690 patients revealed that the blood pressure was recorded in the chart in only 20% of all outpatient visits in the preceeding year.

It was concluded that blood pressures should be determined routinely on all patients attending outpatient clinics of all specialties.

Introduction

Recent evidence has documented the beneficial effects of antihypertensive therapy in the reduction of morbidity and mortality of patients with

The hypertension detection program described was accomplished in the existing out-patient facilities of three hospitals without a large outlay of funds and with the help of specially trained high school students. The study showed that 51% of the adult patients were found to have blood pressures greater than 140 mm. Hg systolic or 90 mm. Hg diastolic.

hypertension^{1,2,3}. It is estimated that twenty-five million Americans have blood pressures that are considered hypertensive^{4,5,6}, and would benefit significantly from effective antihypertensive therapy. Among the first steps to effectively deal with this widespread cardiac risk factor has been the formation of the National High Blood Pressure Education Program and the Recommendations of the Inter-Society Commission for Heart Disease Resources^{7,8}. After effective physician and public education, the next logical step is the identification of the population at risk. The Inter-Society Commission for Heart Disease Resources has emphasized that since hypertension is usually an asymptomatic dis-

order, it is essential to identify persons with elevated blood pressures by screening techniques, either incidental (employment, insurance examinations) or organized⁸. Organized blood pressure screening has been accomplished by mobile units, door to door surveys, and in supermarkets, shopping centers, and churches^{9,10}. Because of limitations of resources, a logical site to begin hypertension screening is in the existing health care resources of the community. An organized hypertension screening program and survey was conducted in the existing outpatient clinics of a city hospital, a community hospital and a university hospital in metropolitan Washington, D.C. and forms the basis of this report.

Methods

The blood pressure screening and survey in hospital outpatient clinics was a pilot project sponsored by the Washington Heart Association and was accomplished with the aid of six high school students working under the direction of a nurse with training in cardiovascular diseases. After undergoing audiometric testing to assure the absence of any hearing impairments, the students were instructed in the determination of blood pressures with a mercury sphygmomanometer according to the recommendations of the American Heart Association¹¹. The

HYPERTENSION DETECTION IN WASHINGTON, D.C.

MROCZEK, WILSON AND FINNERTY

accuracy of the students blood pressure determination was assured by means of a standard testing film^{1,2}, personal observation with a double earpiece training stethoscope, and repeated spot checks of both normal and abnormal values. The students were also given lectures concerning the hazards of hypertension, common hospital vocabulary, the names of frequently used antihypertensive medications, and a general orientation to the hospitals. When the students were sufficiently skilled in auscultatory blood pressure determination, they were assigned to various medical and surgical clinics on a rotating basis. The three hospitals selected for the survey were chosen to cover a broad spectrum of medical practice in the metropolitan District of Columbia area. The survey was accomplished in a large inner-city hospital, an urban university hospital, and a suburban community hospital. Blood pressures were determined and questionnaires were filled out, usually during the interval between the patient's arrival at the clinic and the time he was seen by the physician.

All patients with blood pressures greater than 140 mm. Hg systolic or greater than 90 mm. Hg diastolic were informed of their blood pressure elevation and given a return appointment at a time convenient for the patient. A patient was considered hypertensive if on two re-examinations his blood pressure was greater than 140/90 mm. Hg. Verification of the initial blood pressure could only be accomplished at the city hospital because of logistical reasons. At the time of the initial blood pressure recording, a simple questionnaire was filled out by the student assistant. When available, the hospital records were scrutinized by the nurse for previous blood pressure determinations, past diagnoses, and previous therapy.

Although many clinics claimed to routinely record the blood pressure,

we found that this was the case only in the hypertension, renal, cardiac, birth control and obstetrical clinics. These five clinics were the only ones specifically excluded from analysis in the present study.

Results

A total of 1247 patients were screened for hypertension in the various clinics of the three hospitals surveyed. Of these patients, 637 (51%) were found to have blood pressures greater than 140 mm. Hg systolic or 90 mm. Hg diastolic (table I). None of the patients with normal blood pressures had a past history of hypertension, whereas 53% of the patients with elevated blood pressures had previous knowledge of blood pressure elevations and these percentages were similar in all three hospitals. Of the 336 patients with a known history of hypertension, 67% had received some therapy for "high blood pressure" in the past year. Nineteen percent of the patients given re-examination appointments returned for a recheck of their blood pressure. Of these patients, 84% were found to have persistent elevations of blood pressure and were referred for evaluation and therapy of their hypertension.

A review of hospital records showed that 426 of the 637 patients with elevated blood pressures were previously seen in an internal medicine clinic within the past year; however, only 155 of these patients had a blood pressure recorded in the chart during the preceeding 12 months. Analysis of 690 hospital charts accounting for 4461 clinic visits, showed that blood pressures were recorded in only 20% of the outpatient visits, (24% in the university hospital, 22% in the community hospital and 18% in the city hospital; Table II). Review of 675 visits to the general medical clinic revealed that the blood pressure was recorded in 73% of the university hospital visits, 41% of the community hospital visits, and 34% of the city hospital visits. Of 527 surgical clinic visits, the blood pressure was recorded in only 3.4% of the patients. Further analysis was obtained in eighty-one patients with elevated blood pressures and a past history of a myocardial infarction or a cerebrovascular accident. Most of these patients were being followed at the city hospital (70%). Even though 41 (51%) of these patients were currently on antihypertensive therapy, only 11 (27%) of these patients had their blood pressure recorded in the hospital record in the

TABLE I: Results of Hypertension Screening in Three Hospitals

	City Hospital	Community Hospital	University Hospital	Total (All Hospitals)
No. Patients Screened	1007	110	137	1247
Patients with Elevated Blood Pressures	539	45	53	637
(%)	(54%)	(41%)	(39%)	(51%)
Hypertension Previously Diagnosed (No.)	270	31	35	336
(%)	(27%)	(28%)	(26%)	(27%)
"High Blood Pressure Therapy" within the past year (No.)	178	19	29	226
(%)	(18%)	(17%)	(21%)	(18%)

past 12 months and only 15 of these 81 patients had their hypertension under adequate control (less than 160/100 mm. Hg), (Table III).

Discussion

Recent studies have documented many shocking statistics regarding the therapy of hypertension. In a survey of an industrial population, the percentage of previously diagnosed hypertensives who were receiving antihypertensive therapy has steadily declined from 1967 to 1971¹³. Despite the availability of medical care, numerous deficiencies in the detection, treatment, and control of hypertension have recently been documented by Langfield¹⁴. To combat some of these deficiencies, a massive physician and public education program has been launched with the formation of the National High Blood Pressure Education Program.

The Report of the Inter-Society Commission for Heart Disease Resources has recommended that the first step in the management of hypertension is the detection of the hypertensive individuals via organized community screening programs⁸. Although elaborate hypertension detection programs have had their share of success in the identification of persons with elevated blood pressure, we sought to utilize the existing health care facilities

in the outpatient departments of a city hospital, a community hospital, and a university hospital. The present study showed that 51% of all adult patients attending the various medical and surgical clinics had an elevated blood pressure on initial screening. This high percentage of patients with elevated blood pressures was not surprising, since nearly all of the patients were black and it is well known that blacks have a high incidence of hypertension^{4,5,6}. In the present study, 84% of the persons who returned for verification of the elevated blood pressure were found to be hypertensive on three occasions. The survey reported here was conducted predominantly in the period of time that the patients were waiting to see the clinic physician, and did not prolong the length of time that the patients spent at the hospital on their clinic day. This method of screening appeared to be relatively efficient and an inexpensive way of evaluating nearly 1300 patients in a short period of time.

The chart review which revealed that only 20% of the 4461 clinic visits had a blood pressure determination recorded was shocking indeed, particularly in view of the 51% incidence of elevated blood pressures in this population. Although we excluded several clinics in which blood pressures were routinely recorded, it was still shocking that only one half of patient visits

TABLE III: Analysis of Eighty-one Hypertensive Patients with a History of a Myocardial Infarction or a Cerebrovascular Accident

	No.	%
Blood Pressure Recorded in past 12 months	11	14
Presently on Antihypertensive therapy	41	51
Blood Pressure <160/100 mm. Hg	15	19

in internal medicine clinics had a blood pressure recorded (Table II). All of the clinics evaluated were either run under medical school auspices or in affiliated programs under medical school supervision. Is it any wonder then that recently graduated physicians very often fail to evaluate, treat, or even refer hypertensive patients to appropriate treatment facilities¹⁵?

The effectiveness and accuracy of the students who participated in this study document the feasibility of utilizing specially trained lay personnel in hypertension detection programs. The students were well received by the nursing personnel and physician staffs at most of the hospitals. Although we were satisfied with the accuracy of the blood pressure determinations by periodic spot checks of both normal and abnormal blood pressures, some clinic physicians objected to the "over-diagnosis" of elevated blood pressures. However, since 84% of the patients were found to have persistently elevated blood pressures on two re-examinations (first by a nurse and then by a physician), it seems unlikely that the students were "over-estimating" the blood pressure.

In the study by Langfield¹⁴, 48 of 51 hypertensive patients had visited a primary source of medical care within the past year. A recent Harris survey¹⁶ revealed that 67% of Americans have seen a physician in the past year and 77% had their blood pressure checked

TABLE II: Results of Chart Review for the Previous 12 Months in Three Hospitals

	ALL CLINICS			INTERNAL MEDICINE CLINICS		
	No. Visits	Blood Pressure Recorded		No. Visits	Blood Pressure Recorded	
		No.	%		No.	%
City Hospital	2304	413	18	291	103	35
Community Hospital	609	121	20	155	63	41
University Hospital	1548	378	24	229	168	73
Total (All Hospitals)	4461	912	20	675	334	49

HYPERTENSION DETECTION IN WASHINGTON, D.C.

MROCZEK, WILSON AND FINNERTY

in the past 12 months. However, this same study revealed that 40% of the persons who had their blood pressures checked were never told if their blood pressure was normal or abnormal. The hypertension detection program described in this communication was accomplished in the existing outpatient facilities of three hospitals without a large outlay of funds and with the help of specially trained high school students. There was essentially no disruption of the normal clinic routine and no additional waiting time was incurred by the patients. If all health care facilities (clinics, emergency rooms, private physicians of all specialties, podiatrists, dentists, etc.) would routinely determine the blood pressure of *all* their patients, the need for other types of screening would be minimized. After an elevated blood pressure is recorded, adequate treatment facilities are essential and planning must also incorporate a mechanism for continued follow-up of the newly discovered hypertensive patient¹⁷.

On the basis of this study, it was concluded:

- 1) Approximately half of adult black outpatients attending clinics in a metropolitan area may be expected to have elevations of blood pressure.
- 2) Existing health care facilities could easily and economically function as screening centers for the detection of hypertension.
- 3) Blood pressure determination should be a routine procedure for all outpatient medical visits—both in the hospital and in the offices of private physicians, dentists, podiatrists, optometrists, etc.
- 4) The necessity for routine blood pressure determination and the necessity for identification, documentation and therapy of hypertension must be stressed in medical schools and in house staff training programs.

Acknowledgement

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References

1. Veterans Administration Cooperative Study Group on Antihypertensive Agents: Effects of treatment on morbidity in hypertension: I. Results in patients with diastolic blood pressures averaging 115-129 mm. Hg, JAMA, 1967, 202, 1028.
2. Veterans Administration Cooperative Study Group on Antihypertensive Agents: Effects of treatment on morbidity in hypertension: II. Results in patients with diastolic blood pressures averaging 90-114 mm. Hg, JAMA, 1970, 213, 1143.
3. Veterans Administration Cooperative Study Group on Antihypertensive Agents: Effects of treatment on morbidity in hypertension: III. Influence of age, diastolic pressure, and prior cardiovascular disease; further analysis of side effects, JAMA, 1972, 45, 991.
4. U.S. Department of Health, Education and Welfare: Blood pressure of adults by race and area, United States, 1960-1962. National Health Survey, National Center for Health Statistics Series II, 1964, 5.
5. U.S. Department of Health, Education and Welfare: Blood pressure of adults by age and sex, United States, 1960-1962. National Health Survey, National Center for Health Statistics Series 11, 1964, 4.
6. U.S. Department of Health, Education and Welfare: Hypertension and hypertensive heart disease in adults, United States, 1960-1962. National Health Survey, National Center for Health Statistics Series 11, 1966, 13.
7. Inter-Society Commission for Heart Disease Resources. Atherosclerosis Study Group and Epidemiology Study Group: Primary prevention of the atherosclerotic diseases, 1970, 42, A55.
8. Report of Inter-Society Commission for Heart Disease Resources: Guidelines for the detection, diagnosis, and management of hypertensive populations, 1971, 44, A263.
9. FINNERTY, F. A., SHAW, L. W., HIMMELSBACH, C. K.: Hypertension in the Inner City: II. Detection and Follow-up, 1973, 47.
10. MAXWELL, M. H.: Hypertension, A Functional Approach to Screening, The Hypertension Handbook, Merck, Sharp & Dohme, 1974, 43.
11. KIRKENDALL, W. M., BURTON, A. C., EPSTEIN, F. H., FRIES, E. D.: Recommendations for human blood pressure determination by sphygmomanometers, Circulation, 1967, 36, 980.
12. WILCOX, J.: Observer factors in the measurement of blood pressure, Nurs Res, 1961, 10, 4.
13. SCHOENBERGER, J. A., STAMLER, J., SHEKELLE, R. B., SHEKELLE, S.: Current Status of Hypertension Control in an Industrial Population, JAMA, 1972, 222, 559.
14. LANGFIELD, S. B.: Hypertension: Deficient Care of the Medically Served, Annals of Internal Medicine, 1973, 78, 19.
15. MROCZEK, W. J.: Diagnosis and treatment of hypertension, American Heart Journal, 1973, 85, 718.
16. HARRIS, L. and ASSOCIATES, INC.: The Public and High Blood Pressure, A Survey Conducted for the National Heart and Lung Institute, Study No. 2313, 1973.
17. SHULMAN, N. B.: An Effective Screening and Follow-up Program, The Journal of Urban Health, 1973, 2, 2, 18.

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Torsion of The Testis and Its Appendages

GLENN W. GEELHOED, M.D.

Abstract

Patients who present with pain, swelling, and erythema in the scrotum should be carefully examined to determine an accurate diagnosis. Torsion of the testis presents as a tender indurated testis, and if that is present, or cannot be confidently excluded, prompt surgical exploration of the scrotum should take place. If the patient is examined early, and on physical examination the tenderness and swelling are localized to the upper pole of the testis which itself feels normal, and transilluminating the scrotum with the skin drawn taut reveals a dark shadow at the upper pole of the testis, a clinical diagnosis of torsion of the appendix testis can be made. Treatment of torsion of the appendix of the testis or epididymis may be symptomatic if this diagnosis is made accurately when a patient is seen early. Inflammatory conditions of the testis and epididymis are medically managed and a search is made for an underlying cause of the orchitis or epididymitis.

Pain, swelling, and erythema of half the scrotum are common presenting complaints in young boys. There are two structural deformities that can give rise to these symptoms in addition to inflammations of the testis and its appendages. Differential diagnosis is important since the treatment is different if the condition giving rise to the presenting symptoms is inflammatory,

If there is physician delay due to an incorrect diagnosis or inability to exclude torsion of the testis, a potentially viable testis which may have first presented when its venous drainage was compromised after torsion might progress to infarction under physician observation.

torsion of the testis, or torsion of the appendix testis.

The testis itself is fixed in its position in the scrotum by the tunica vaginalis along the full length of the epididymis. When this fixation is deficient, the testis has several degrees of freedom of movement predisposing to torsion within its sac in the scrotum.

The appendix testis is a sessile or pedunculated attachment on the upper pole of the testis below the head of the epididymis. The appendix testis (hydatid of Morgagni) is a vestigial remnant in the male of the embryologic Mullerian duct. The appendix testis is present in 92% of males according to one autopsy series¹ and a similar appendix was found arising from the epididymis testis in 34% of autopsied males. Eighty-four percent of these appendices testes were pedunculated and 100% of the appendices epididymis were pedunculated,

thereby allowing torsion of the appendix to occur. On rare occasions, there may be multiple appendices. An example of such a case encountered during routine herniorrhaphy is seen in Figure 1 with three pedunculated appendices, two arising from the epididymis and one from the testis.

Patient Series

One hundred thirty-one patients presented, over a six year period, with swelling and pain in the scrotum. One hundred seven of these patients had torsion of the testis or an appendix; 58 of these involved the appendix and 49 the testis. The remaining 24 patients had an inflammatory process involving the epididymis and/or the testis. The differential diagnosis between these three conditions is difficult but is important because the outcome frequently depends on whether or not prompt surgical exploration is carried out. If a definite diagnosis cannot be made to confidently rule out torsion of the testis, prompt surgical exploration of the scrotum is indicated.

Operations performed for torsion of the testis continue to have a low salvage rate. Once torsion occurs venous obstruction and subsequent compromise of arterial blood supply lead to necrosis within a matter of hours.² If there is physician delay due to an incorrect diagnosis or inability to exclude torsion of the testis, a poten-

TORSION OF THE TESTIS AND ITS APPENDAGES

GEELHOED

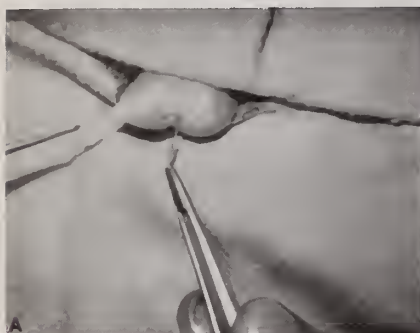


FIG. 1. Appendices of testis and epididymis as seen in patients undergoing routine herniorrhaphy. A. An appendix of the testis and an appendix of the epididymis as seen in a normal scrotum. B. Another normal specimen with two appendices epididymis and one appendix testis.



tially viable testis which may have first presented when its venous drainage was compromised after torsion might progress to infarction under physician observation. When finally explored the necrotic testis cannot be salvaged (Figure 2A and B). Treatment of torsion of the testis is immediate operation and correction of the deformity.

Torsion of the Testis

Torsion of the testis most frequently presents with the sudden onset of pain. Sixty percent of our patients reported the sudden onset of pain whereas in the remaining 40% the

onset was gradual. The pain may be referred to the inguinal area. Vomiting was noted in only 15% and pallor, sweating, weakness, anorexia, and nausea were seen in only a few older patients. Five percent of the torsions occurred in undescended testes. Thirteen newborns were seen with extravaginal torsions (that is, torsion of the spermatic cord) and all have had gangrenous testicles even though some were operated upon shortly after birth.³

Swelling, tenderness, and definite firmness and induration of the involved testicle were present universally in this series. Erythema of half of the scrotum was present in 50%. A physical sign in some cases of testicular torsion is that the testis may lie in a high position with its long axis horizontal rather than vertical.

Inflammations

If a patient is seen early enough to definitely exclude the diagnosis of testicular torsion, non-operative management may be attempted, with treatment directed toward the symptoms after a definite diagnosis has been made. A careful search for the cause of the inflammatory conditions is mandatory since epididymitis and orchitis are unusual in boys without some underlying anatomic or physiologic abnormality. Of 24 patients in this series who had the diagnosis of epididymitis or orchitis substantiated, 15 were found to have an underlying cause such as leukemia, mumps, local sepsis or multiple genitourinary anomalies. The truly inflammatory conditions of the testis and epididymis may be treated with control of symptoms by rest, elevation of the scrotum, analgesics and anti-inflammatory drugs, and specific antibiotic therapy if a bacterial etiology is confirmed.



FIG. 2. Torsion of the testis. A. A testis that has undergone torsion and ischemia suspended from the cord seen at the top of this illustration. B. Torsion of another testis which has advanced to complete testicular infarction.



Torsion of the Appendix Testis

Torsion of the appendix testis generally presents with sudden onset of pain in the scrotum similar to torsion of the testis. (Figure 3A and B) However, 45% of the patients give a history of either gradual onset of pain or intermittent pain with appendicular torsion. Twenty-five percent of our patients had onset of pain following trauma, heavy exertion or sports.



FIG. 3. Torsion of the appendix testis. A. Torsion of an appendix testis leading to appendicular infarction. B. Gangrene of another appendix testis following appendicular torsion.



Torsion of the appendix testis is most common in boys aged eight to 13 and is rare under age three. Four of the patients who had had previous herniorrhaphy developed appendicular torsion on the same side several years later. One of the patients developed torsion of the opposite appendix testis one and one-half years following the original torsion of the appendix testis on the first side.

On physical examination when seen early, torsion of the appendix testis may show tenderness, erythema, and swelling localized over the upper pole of the testis. Thirty percent of the patients in this series were seen at this stage. If the examining physician stretches the skin taut over this area

and transilluminates the scrotum, a blue-black gangrenous appendix testis may be seen as a dark shadow at the upper pole of the normal testis which gives a reddish-pink tinge when transilluminated. In the later stages of torsion of the appendix testis, the appendix may become gangrenous and cause a general inflammatory response throughout the testis, epididymis and scrotum making differentiation from testicular torsion impossible. Excision of the appendix testis is curative before the torsion leads to much ischemic pain, but infarction of the appendix testis also is curative.

Prevention

Prevention of these diseases involves education of parents by pediatricians and family physicians to the potential significance of scrotal swelling in children. Also, the undescended or ectopic testis frequently has abnormal fixation and a corresponding higher incidence of torsion.⁴ Correction of the location of the ectopic testis and fixation in the scrotum may prevent torsion of these abnormally located testes. If a patient has previously had a torsion of one testis which resulted in its infarction, fixation of the opposite viable testis may be considered. In this series of patients, only one patient returned with a torsion of the opposite testis.

Torsion of the appendix testis can be prevented if, during herniorrhaphy, the surgeon mobilizes the testis in the inguinal wound and excises appendices of epididymis and testis. This routine practice would have been significant in this series of patients in which four patients previously operated upon for hernia repairs returned some years later for operations for appendicular torsion. It is important when using the inguinal incision to carefully replace the testis in the scrotum since one of our patients required an orchiopexy

one and one-half years following operation for torsion of the appendix testis in a testis that was fully descended.

References

1. ROLNICK, KAWANOUE, SZANTO, RUSH: Anatomic Incidents of Testicular Appendages, *J. Urol.*, 1968, 100:755.
2. SMITH: Cellular Changes From Graded Testicular Ischemia, *J. Urol.*, 1955, 73:355.
3. LONGINO: Torsions of the Spermatic Cord in the Newborn Infant, *New England Journal of Medicine*, 1955, 253:695.
4. YANICELLI: Torsion of Ectopic Testis in Children, *Archives of Urug. Med.*, 1948, 33:60.

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THE VIEW BOX

**Prepared by
The Department of Radiology
Washington Hospital Center**

A 43 year old male is admitted with left leg pain following a car accident. Physical examination reveals a swollen tender left knee with a weak dorsalis pedis pulse.



How would you proceed?
(for diagnosis see page 456)

SPECIAL ARTICLE

HMO—Friend or Foe?

HORACE W. BERNTON, M.D.

Background

"HMO" (Health Maintenance Organization or Comprehensive Pre-paid Health Care) is an anathema to many physicians and an enigma to many legislators and the public. What is the history of this concept of financing health care, and where does it fit into the scheme of things? To the physician, is "HMO—Friend or Foe?"

Most Medical Care Foundations are currently committed to implementing professional standards review organizations (PSRO) by developing standards for medical care, by reviewing utilization of medical care, and by assessing the quality of care delivered to beneficiaries of Government-sponsored programs. To date, many Foundations have not fully addressed the multifaceted problems of access to medical care. These include such factors as availability of physicians, systems of referral, transportation, and financing of medical care. I wish to discuss methods of financing medical care, because financial barriers to access are very much the concern of comprehensive foundations.

Basically, the following alternatives are available to finance medical care:

1. Partial or full payment by individuals on a fee-for-service basis.
2. Under the auspices of commercial carriers or Government plans (Medicare and Medicaid), indemnification of part of the risk of

...I have attempted to define objectively HMOs, outline societal pressures for HMO development and offer a summary of arguments pro and con. I favor Medical Care Foundations playing an active role in testing the efficacy of pre-paid comprehensive medical care.

medical expenditure. In no situation are all costs covered and rarely are preventive health services provided.

3. Pre-paid comprehensive medical care plans, where groups of beneficiaries contract with groups of physicians to receive comprehensive medical care for an established prepaid premium. Preventive health services are provided.

This last (pre-paid comprehensive medical care) has acquired the generic label "Health Maintenance Organization," or the acronym "HMO." There has been confusion in the minds of the public, legislators, and physicians as to the meaning and impact of the HMO concept; one of the problems is that the term "HMO" comprises a large spectrum of service plans and organizations. Because of public attention to pre-payment, Medical Care Founda-

tions have been active in studying the feasibility of sponsoring demonstration pre-payment plans. It is appropriate to attempt to place this concept in proper perspective and evaluate its effect on physicians' professional lives. The following paragraphs will focus on societal pressures for pre-paid plan development, the pros and cons for patients and physicians alike, the position of American Medical Association (AMA) and the American Association of Foundations for Medical Care (AAFMC) position, Medical Care Foundation activities in this field, and my personal position. I hope that the information presented should allow each of us to make informed decisions on the pre-payment issues with which we surely will be confronted.

Types of Pre-paid Plans

1. The classic HMO models are the pre-paid closed group setting exemplified by the Kaiser-Permanente and the Group Health Association of Washington, D.C. The former operates its own hospitals and the latter has only ambulatory care facilities and uses existing hospitals. In both instances, physicians are salaried and the free choice of physician limited, but care is comprehensive. Generally, crisis mental health coverage is offered. Periodic health maintenance care is

HMO—FRIEND OR FOE?

BERNTON

available to enrollees. Testimony to the public's acceptance of this form of pre-paid care is indicated by the five to eight million people currently enrolled in group practices throughout the country.

2. Medical training centers such as Harvard, Yale, Johns Hopkins, Georgetown and George Washington are mobilizing HMOs about their teaching and affiliated hospitals and establishing community ambulatory care centers.
3. Federations of physician-run group practices are organized with the community, such as the Health Insurance Plan in New York (HIP) which has 300 full-time physicians and 800 part-time physicians and 770,000 subscribers. This plan was set up in 1947. Hospitalization is handled under a separate policy, which has many disadvantages from an overall management point of view.
4. OEO—Community Health Centers have been attempted but these have met with limited success. One such effort has been in Baltimore; an outgrowth of the activities of medical planning and community groups, the Regional Medical Program and Johns Hopkins University. It is funded by the State of Maryland and some Federal funds and provides ambulatory care for about 2,000 economically disadvantaged in Baltimore.
5. In California, particularly in response to public demand, small physician groups are sponsoring HMOs. Because of their small size and lack of resources, cash reserves and bargaining power their effectiveness is limited.²
6. Medical Society Foundations³, such as those at San Joaquin and

Sacramento⁴ in California and Clackamas County in Oregon, were founded in response to economic pressures created by the development of closed panel group practices. In each of these foundations, models of so-called "Open-ended HMOs" or "Community Health Plans" or "Individual Practice Associations" (I.P.A.), as they are now called, have evolved and have interfaced with those programs which serve Medicaid populations and unions and commercial carriers, including the "Blues." In this setting physicians are paid by the Foundation on a fee-for-service basis at rates they establish, and appropriate arrangements are made for hospitalization. In a system which, in effect, allows unlimited patient access and physician utilization of medical services, there has to be some method of controlling abuses. To accomplish this, the foundation's peer review system is utilized. Also, there must be mechanisms available for physician and patient appeals. It is important to note that while such a system of health care could be marketed and underwritten by a commercial carrier, it is physician-controlled. Schedules of benefits and fees, standards of care, and criteria for peer review are developed by the foundation. Commercial carriers might underwrite or take the risk, but this increases costs so that foundations themselves frequently go "at risk" and in effect underwrite the plan. When foundations are "at risk" they generally compensate physicians at about 95% of their usual, customary and reasonable fee. Five percent may be held in escrow to guarantee the integrity of the fund.

In some instances risk above this 5% is reinsured with a commercial carrier. This, of course, limits physicians' risk to 5 cents on a dollar. If the actuarial estimate is valid, then physicians performing the service are compensated at 100% of usual, customary and reasonable fee. To date, the record of foundations is excellent and physicians have rarely been called upon to finance a deficit. Such pre-paid comprehensive plans offered by medical foundations provide the private sector an opportunity to gather data on utilization rates and costs, utilize innovated access techniques, to identify barriers to care, and to improve the system of medical care available to the enrollees.

Pressures for HMO Development

The basic concept of comprehensive pre-paid medical care received national attention in 1970 when John G. Veneman, Under-Secretary of the Department of Health, Education and Welfare, and Dr. Paul Ellwood, his consultant, presented it to Congress. They directed attention to several formats: the closed panel "HMO" (Kaiser-Permanente), the community "HMO" (Clackamas County Medical Foundation), and the medical school HMO (Columbia). They had thought that great savings could accrue to the Medicare program by utilization of pre-paid programs. Since then, there have been a number of bills presented to Congress to encourage HMO development. However, at this point in time there are three major developments on the national scene that one should recognize: First, the Department of Health, Education and Welfare in 1971 passed legislation which created an HMO office that made available \$18 million for HMO planning and devel-

opment; Second, the passage of H.R. 1 last fall extended an HMO option to 25 million Americans over 65 who are Medicare beneficiaries. It is only recently that Gordon McLeod, M.D., then Director, HMO Service of HEW, recognized the validity of a broader HMO concept to include Foundation plans, stating that "physicians, practicing predominately as individuals, or in group practice, can develop more or less formal organizational relationship among themselves and with hospitals and enrolled populations and can apply mechanisms of review which have many of the objectives usually only attributed to pre-paid practice."

For the third major development, Senator Kennedy (D-Mass.) introduced a \$5 billion HMO development bill which gave almost no recognition to Foundation-sponsored HMOs until it was amended by Senator Dominick (R-Colo.). This bill, as amended (Senate Bill 14)⁵ subsequently passed during the 1973 session. On September 11, 1973, the Hastings version of the Rogers-Roy HMO bill (H.R. 7974) was passed. The bill, originally submitted by William Roy, M.D. (D-Ks.) and Paul Rogers (D-Fl.), has been a format on which other bills have been built. AMA, organized labor, the health care industry, and HEW have all been working to have the HMO bill reflect their needs.

On December 29, 1973 Congress passed, and the President signed, compromise legislation (Public Law 93-222) which provides a great stimulus for HMO development. It authorizes \$325 million to be spent in the next five years for HMO start-up. It also provides that any employer of twenty-five persons or more must offer, if it is available, a "certified" pre-paid alternative to his employees. It should be noted that Foundation-sponsored pre-paid plans (IPA's) do qualify along with closed panel plans, for benefits under the law. Also, the

law under certain circumstances pre-empts State legislation which discourages or makes impossible HMO or IPA development.

Other Pressures

Boyd Thompson, Executive Director of AAFMC points out: "... it is no longer hypothetical that the American health care delivery system will change. It must and it will change...", and he goes on to elucidate the societal pressures for change impacting on the profession. Pre-paid comprehensive health care has caught the public's attention. To the enrollee, the concept of his being able to budget down to the very last dollar the cost of his medical care is a profound advantage. Also, if he can get what, to his mind, is adequate high quality medical care and preventive services, the concept becomes more appealing. He will be even more enthusiastic if he can select his own physician and hospital. Evidence of public acceptance of comprehensive pre-paid care is the support given by such major philanthropic institutions as Ford, Rockefeller, and the Johnson Foundations.

Another important pressure for HMO development is from the insurance industry. Companies such as Connecticut General are committing huge sums to front end HMOs, mostly of closed panel formats such as the Columbia Medical Plan. The national strategy of the Blue Cross Association was elucidated at a recent HMO conference sponsored by The American City Corporation in August of last year. The spokesman stated that the objective was the founding of 300 HMOs by 1977. The role they saw was to organize and control their own pre-payment plans. It was further stated that 55 of 70 Blues' plans in the United States are at some point of HMO development, and that they are involved in 20 operational HMOs at

this time. These include associations with such plans as HIP of New York, Group Health of D.C., the Harvard HMO (Massachusetts Plan), the Detroit program which grew out of United Mine Worker's plans, and with programs in Rochester, New York, and Rhode Island. Furthermore, there is a commitment of reserve funds for HMO development. There is every evidence that the Blues are making a major commitment to capture a large part of the HMO market, moving in the direction of funding closed and open panel HMOs. In Southern California with their "CommuniCare" plan, Blue Cross is marketing a pre-paid plan utilizing existing multi-specialty groups as providers, similar to HIP in New York, but they do recognize the Medical Care Foundations as a "group." On the other hand, in Long Island, New York, they are marketing a community HMO where all services will be delivered at one hospital, the Long Island Jewish-Hillside Medical Center. In the Washington Metropolitan area, Blue Cross, via Group Health Association, Georgetown and George Washington Universities, is involved in underwriting and marketing closed panel HMOs. Blue Cross is developing a market. How many of you have heard the radio advertisement, "What's an HMO, Daddy?" and further "... That you can go to one place to get all your health care." Blue Shield has announced that a comprehensive package of benefits, emphasizing ambulatory care is under intense study.

Recently Donald S. Farver, President of Group Hospitalization, Inc. and Mr. Victor M. Brian, President of Medical Service of D.C., stated their willingness to enter into a dialogue with physicians of the Metropolitan area regarding comprehensive health insurance.

Thus national and local pressures for the private sector of medicine to

HMO—FRIEND OR FOE?

BERNTON

develop pre-paid alternatives are, to my mind, overwhelming. Federal legislation provides increased marketing opportunities for HMOs and locally there is an intensive marketing effort being mounted by all three closed panel programs. The foundations must be in a position to compete.

Washington Metropolitan Area

There is a great deal of activity in the Washington Metropolitan area regarding the expansion of existing HMOs and planning and study for future pre-paid plans. The Group Health Association of D.C. has opened a large ambulatory care facility in Montgomery County and has several small out-patient facilities strategically placed in suburban Maryland. There is ample evidence that they plan to and are currently engaged in a large marketing operation in Washington and suburban Maryland. Columbia Medical Plan in Howard County, Maryland, has opened its own hospital. Model HMOs now surround George Washington and Georgetown Medical Schools. There is definite evidence that Georgetown is looking to Prince Georges County and Montgomery County as future markets and is opening an ambulatory care center in Kensington, Md. this fall. With forthcoming Federal programs there will be strong incentives for one or more hospitals in the Metropolitan area, particularly if they have strong medical school affiliations, to organize and market a comprehensive pre-paid health plan. Also, with the passage of HMO legislation (P.L. 93.222) is there strong incentive, as in California, for moderate or large-sized group practices to form HMOs.

Montgomery and Prince George's County Foundations participated in a Medicaid-HMO feasibility study. A detailed study revealed that it was

not economically feasible to develop a capitation⁶ rate which would not significantly increase total Medicaid dollars spent in these two counties. It was suggested that increased expenses generated by improved access to care and payment of reasonable physician fees would far outweigh any savings that might be derived from a hospital certification program. Prince George's County Foundation will probably attempt to negotiate a rate with the State that is economically feasible, but it is doubtful that the State will want to increase its Medicaid expenditures in Prince George's County. The Board of the Montgomery County Medical Care Foundation voted to communicate to the State the results of its study and will not attempt any negotiations with the State but will wait and see the outcome of the Prince George's County Foundation effort. The National Capital Medical Foundation (of D.C. Medical Society) is about to study the feasibility of model pre-paid plans. Regional Medical Program established an HMO Committee called the Washington Area Technical Committee on Health (WATCH) which was designed to give technical assistance to emerging HMOs in the metropolitan area. It started establishing "guidelines" and review procedures, but the Montgomery County Foundation had a great deal of constructive input into its formulation so that its scope is advisory only. At this point in time it is hardly a viable committee and its impact is limited.

The Foundations of Metropolitan Washington have organized themselves as the "Metropolitan Washington Federation of Medical Foundations, Inc. This organization consists of representatives of the Foundations from the District of Columbia, Montgomery County, and Prince Georges County, as well as those interested in foundation activities in Virginia. Its goal is to develop close lines of communication

for all foundations in the Metropolitan area. This was felt necessary so that foundation positions could be elucidated and consolidated and not be fragmented when programs are developed and negotiations begin with insurance carriers. Also there is a need for a structure to coordinate plans which might be implemented.

The Federation sponsored a workshop to develop an overall strategy regarding IPA development. John J. Boardman, Jr., and Robert Eilers of the American Health Maintenance Advisory Corporation joined the Federation in their deliberations. The following questions were asked:

1. How is a negotiating position developed with regard to schedule of benefits, schedule of fees, standards of care, standards of peer review and mechanisms of peer review?
2. Is the organizational structure or in-house capability available for performing these tasks.
3. Is there a need for outside consultation and expertise?
4. Is there a need for an advocate in negotiations with commercial insurance companies which are considerably experienced in such matters?
5. How would such an effort be funded?

The Federation subsequently established a task force on IPAs of which I am chairman. The task force and the Federation have formally adopted the motion that the Federation should move to enhance IPA development among foundations in the Metropolitan area. This will be done by identifying areas of cooperation and coordinating activities of the individual IPAs. Implementation will be facilitated by cooperating in feasibility studies, benefit package design, utilization of management consultants, legal and actuarial consultation, systems design, marketing, and selection of underwriters.

American Medical Association (AMA) Position

The AMA's position is clearly outlined in an analysis "HMO as seen by the AMA," published in June, 1972. In summary, the AMA supports a pluralistic approach to the delivery of medical services and accordingly does not oppose HMO development *per se*. However, it does not see HMOs as a panacea because there are not sufficient data regarding cost effectiveness, quality of care, and physician acceptance. The AMA was involved in an immense program of lobbying to reduce the impact of the final HMO bill recently passed by Congress. It will offer no reprisals against those involved in HMO development. The AMA has stated as long ago as 1959 in the so-called "Larson Report," that individuals should not only be afforded free choice of physician, but also the privilege to select the system of medical care preferred.

American Association of Foundations for Medical Care (AAFMC) Position

Leaders in the Medical Care Foundation movement emphasize, as does the AMA, the necessity for a pluralistic health delivery system, but take a far more progressive position in regard to prepayment of medical care. While AMA will "wait and see," AAFMC feels that we, the profession, should play a more active role in developing pre-paid alternatives, so that we can design the program that we feel best fits needs of the community and our desires. Then we can design the experiment, collect the data, and be the active force for constructive change.

Summary "FOR" AND "AGAINST"

In general, those who argue *in favor* of pre-paid comprehensive care hold that:

1. Cost is predictable.
2. HMOs are cost effective. Ernest Saward, M.D., Professor of Social Medicine, University of Rochester, a long-time student and advocate of pre-paid health care, argues that the data are in and there is no doubt as to the cost effectiveness of HMO programs and that high quality care can be guaranteed.
3. There are great savings in over-all health expenditures, primarily because HMOs emphasize ambulatory care alternatives for hospitalization.
4. There is great incentive for physicians to keep the patient well.
5. Enrollees are assured adequate preventive care.
6. The consumer can have a role to play in the design of his health system.
7. Foundations add: The HMO model can be used as one facet in a system of health delivery which can impact on access, drug usage and quality care and still do this in a setting of free choice of physicians and payment to physicians on a fee-for-service basis.

Major concerns of those who argue *against* HMOs are:

1. It opens doors to the destruction of the physician-patient relationship.
2. It is a device to get "a foot in the door" for socialized medicine.
3. All the data are not in. In contradiction to Saward's argument, the AMA holds that before the HMO concept receives widespread support and national implementation much more study is indicated.
4. Because in many instances the physician is "at risk", if the program is not financially viable, his incentive may be to attempt to cause savings which may be a deterrent to maintenance of high quality care.
5. Consumers should not have a controlling role in any organization dedicated to health delivery.
6. With pre-payment there will be over-utilization of services by enrollees; witness Sidney Garfield and his discussions of the "worried well."
7. I have heard other arguments that I have not seen in print, such as: "Look at the Blues; they started out as the 'physicians own program.'" With physicians offering the plan and also bearing the responsibility of attesting as to quality of care there is a built-in "conflict of interest."

Personal Position

To this point in this paper, I have attempted to define objectively HMOs and outline societal pressures for HMO development and to offer a summary of arguments pro and con. I favor the Foundations playing an active role in testing the efficacy of pre-paid comprehensive medical care and agree with the arguments presented for HMO development. This is consistent with the position outlined above by the AAFMC which is also consonant with the AMA attitude of that this not a proven experiment. Regarding the arguments presented against HMO development, this commentary relates solely to Foundation-sponsored IPA's.

1. Foundation-sponsored pre-paid plans (IPA's) in no way infringe on the physician-patient relationship since patients will be afforded free choice of physician. Physicians are not bound to accept any particular patient.
2. If the profession is not progressive and does not respond to the pressures outlined above to de-

HMO—FRIEND OR FOE?

BERNTON

velop pre-paid alternatives and develop the needed data for improving the system of health delivery it will be done by Government fiat.

3. While all the evidence is not complete, particularly in regard to IPA's, there is a large body of evidence that Saward presents which is quite convincing. The best evidence we can obtain is by designing the prepaid experiment ourselves, implementing it locally, gathering our own data and doing our own evaluation.
4. I have every confidence that the foundation peer review process will be able to carry out its charge. Guidelines will be carefully drawn and published. The review process (PSRO) will be subject to public and government scrutiny. This overcomes the burden of the physician "being at risk" and having a "conflict of interest."
5. Over-utilization is a problem in the day-to-day practice of medicine. It is not unique to pre-payment plans. We have to deal with it daily when patients make what may seem to be unwarranted demands. An interesting case in point was a study performed recently by Group Health Association of D.C. in which, when it offered crisis mental health care, it was able to cut down more than proportionally on medical care utilization. Let's avoid such arguments as "Look at the Blues." I don't know what that means—perhaps the implication is that we will get locked into a consumer dominated program. Haven't we learned our lesson and can't we use this foresight to keep consumer input in proper perspective?

I have had the privilege of being a volunteer member of a team which

studied the feasibility of implementing a closed panel HMO with an open staff hospital. At that time, which was before the concept of Foundation-sponsored pre-paid programs had gained impetus, I was thinking in terms of the advantages of the entire medical community acting as the group. The study showed that such a program, both because of start-up costs and county-societal characteristics, was not feasible. The study is published and is the source of some of the best demographic information to date on Montgomery County.

From this activity, I gained an early experience in medical systems, health planning and at the same time, unfortunately, a label as one who would "involve us all in an HMO." As I have described, there are HMOs and IPAs. Regarding pre-paid care, I believe we are in exactly the same position as we were before the Bennett Amendment to H.R. 1 was passed; that we must prepare for the impact of legislative remedies on our private practice, also we must deal in a realistic manner with economic pressures for the private sector of medicine to offer pre-payment alternatives. I believe, if it is economically feasible, Foundations should study and gain experience with pre-paid comprehensive health care models. Then we will have the experience and data and will be able to know what course to chart. FOUNDATIONS CAN THEN AFFORD THEMSELVES THE ALTERNATIVE, SHOULD IT BE FAVORED BY THEIR MEMBERS, TO OFFER PREPAID PLANS FOR ALL THOSE WHO DESIRE THEM. THIS IS VITAL SO THAT WE WILL BE ABLE TO COMPETE WITH CLOSED PANEL PLANS—AT THE SAME TIME, WE AS INDIVIDUALS CAN CONTINUE TO OFFER SERVICES TO THOSE WITH INDEMNITY INSURANCE. THUS OUR PLURALISTIC SYSTEM IS PRESERVED.

References

1. This essay does not necessarily represent the viewpoint of the Board of Trustees or the membership of this organization.
2. A number of the problems facing this type of HMO are described in the September 17, 1973 issue of *Medical Economics*.
3. See "Letters to the Editor", *The Evening Star*, October 28, 1972.
4. Sacramento Open-Ended HMO is discussed in October 1973 issue of *Medical Economics*.
5. See "Letters to the Editor" for a more detailed discussion of the Kennedy Bill.
6. "Capitation" refers to a specific fee, per enrollee per year based on averaging health risk which is pre-paid.

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Bilateral Successive Adrenal Pheochromocytoma With Complicating Essential Hypertension

NOEL M. DOROMAL, M.D. AND PHILIP MIDDLETON, M.D.

Abstract

A patient with bilateral successive adrenal pheochromocytomas was treated with total adrenalectomy.

Postoperative hypertension was diagnosed as "essential hypertension" after exhaustive diagnostic work-up. The patient was placed on lifelong steroid replacement and antihypertensive medication.

Introduction

Paroxysmal hypertension due to pheochromocytoma was first reported by Labbe in 1922¹. C. H. Mayo reported the first successful operative removal and relief of hypertension due to pheochromocytoma in 1927². Rabin demonstrated an epinephrine-like substance in pheochromocytoma in 1929³. As a cause of hypertension pheochromocytoma accounts for only a small percentage of patients with hypertension, variously estimated at 0.1% to 0.7%. Of these only 15% of adult patients have bilateral or recurrent pheochromocytoma and only 10% to 20% have associated essential hyper-

Recognition of pheochromocytoma is important; removal of the tumor improves or cures the hypertension. Ten to 15% of the tumors are malignant. Unrecognized pheochromocytoma can produce shock and death after minor trauma or after surgery for unrelated conditions.

tension⁴. This case report concerns the very rare occurrence of bilateral successive adrenal pheochromocytomas with essential hypertension in a single patient.

Case Presentation

A 34 year old obese black woman was seen in the outpatient department because of severe headaches associated with sweating, shortness of breath and palpitation. She was first noted to be hypertensive at age 18 and was unresponsive to medication. In 1968 she

was admitted to a neighboring hospital for similar complaints. Work-up showed elevated urinary vanillyl mandelic acid and catecholamines on several occasions. Intravenous pyelogram showed a mass in the right adrenal area. A right adrenal pheochromocytoma was removed through an abdominal approach; exploration of the abdomen failed to demonstrate another tumor. The blood pressure reverted to normal and the patient was asymptomatic for two years but when seen at our clinic was severely hypertensive.

Physical examination on this admission showed a blood pressure of 190/150 and a pulse rate of 120 per minute. The thyroid gland was not enlarged. The lungs were clear. The heart showed a grade I/VI systolic ejection murmur and an S₄ gallop. Light palpation of the abdomen produced sweating, headache and markedly elevated blood pressure.

Laboratory data included normal thyroid function studies and chest X-ray. The intravenous pyelogram showed a 2 cm defect on the upper pole of the right kidney. There was a

PHEOCHROMOCYTOMA WITH ESSENTIAL HYPERTENSION

DOROMAL AND MIDDLETON

pelvic mass producing a defect on the superior aspect of the urinary bladder. Blood sugar determinations varied from 170 to 225 mg%, the calcium was 10.3 mg%, blood urea nitrogen 15 mg%, creatinine 1.0 mg%, white blood cell count 12000 per cubic mm, hemoglobin 14 gms. The serum cortisol was 18.6 mg%. Urinary metanephrine was 6.1 mcg/gm creatinine, norepinephrine 92.8 mcg/gm creatinine, epinephrine 233.2 mcg/gm creatinine (table 1). Regitine (phentolamine) test, using 2.5 mg intravenously, led to a decrease of the blood pressure from 190/150 to 140/90. Abdominal arteriography showed a six centimeter mass in the right pelvis supplied by the inferior mesenteric artery. The defect of the upper pole of the right kidney was compatible with a cyst. The renal arteries were normal. No mass was detected in either the right or left adrenal area. A pheochromocytoma of the organ of Zuckerkandl was suspected.

The blood pressure was controlled with dibenzylamine 20 mg every eight hours. Propanolol was added to the regimen because of persistent tachycardia. Preoperative preparation included a blood volume measurement which showed a contracted red cell volume and an expanded plasma volume. Because of the history, the positive chemical tests, and the findings on arteriogram the patient underwent an exploratory laparotomy.

A radial arterial catheter and a central venous catheter were inserted prior to induction of anesthesia. A 30 mm Hg systolic rise of the blood pressure occurred during induction. Through a left paramedian incision the pelvic area was explored. No mass was found except for a slightly enlarged uterus. Attention was focused on the left adrenal area where palpation produced marked elevation of the blood pressure (table 2); dissection uncovered a left adrenal mass measuring 4 x 8 centimeters. The blood pressure fell precipitously after the left adrenal gland was removed (table 2). Fluids were infused and the blood pressure was maintained at 110-130 mm Hg systolic level without the use of any vasopressor agent. Exploration of the right adrenal area and the rest of the abdomen did not reveal a second tumor nor was there further elevation of the blood pressure. One gram of solucortef was given intravenously during the operation. At the conclusion of the procedure the blood pressure became elevated and the central venous pressure rose to 23 centimeters of water. The central venous pressure decreased to 12 centimeters of water after Lasix was given intravenously.

The blood pressure was below the preoperative level during the immediate postoperative period. However, two days later the hypertension recurred. This time there were no subjective manifestations accompanying the

hypertension. Regitine test and urinary vanillyl mandelic acid were normal. No metanephrine was recovered in the urine (table 1). Histopathologic examination of the adrenal gland confirmed the clinical diagnosis. Renal scan showed normal kidney vasculature. The patient was felt to have "essential hypertension" and required anti-hypertensive medication to control the blood pressure. She was discharged completely asymptomatic with steroid replacement therapy.

Discussion

Recognition of pheochromocytoma is important; removal of the tumor improves or cures the hypertension. Ten to 15% of the tumors are malignant⁶. Unrecognized pheochromocytoma can produce shock and death after minor trauma or after surgery for unrelated conditions^{5,7}.

In making the diagnosis of pheochromocytoma, Gifford *et al* note that on the basis of clinical findings the diagnosis of pheochromocytoma was suspected in 65 of 76 patients in their series before any confirmatory tests were ordered. Twenty per cent of the patients were referred to these authors with the diagnosis of pheochromocytoma. Approximately 50% of these patients showed paroxysmal activity. Palpitation, excessive perspiration and headache were the most common symptoms. Characteristically the headache was abrupt, severe and of short duration⁸.

Although most patients with pheochromocytoma were thin, this patient was obese but had the full-blown syndrome associated with a functional pheochromocytoma. Highly suggestive were the laboratory and physical findings which constitute the triad of H's: hyperglycemia and hypermetabolism without hyperthyroidism.

Preoperative, intraoperative and postoperative management is compli-

TABLE 1: Summary of Diagnostic Laboratory Tests

Test	Normal Values	Preoperative Values	Postoperative Values
Vanillylmandelic acid/24 hr	2-10 mg	4.4 mg	3.0 mg
Catecholamines/24 hr	10-150 µg	326 µg 181 µg	124 µg
Metanephrine/24 hr	0-1.5 µg	6.1 µg 4.0 µg	none

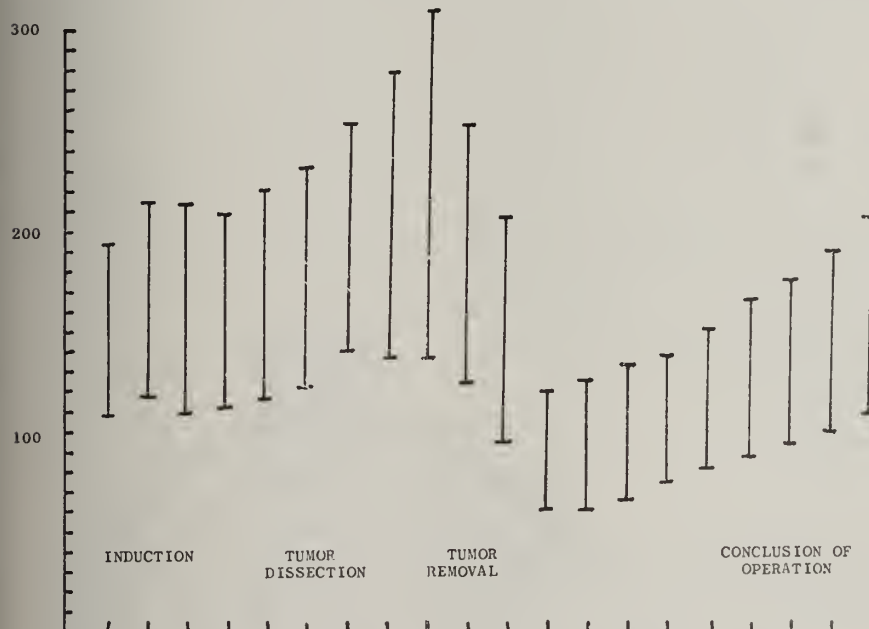


TABLE 2. Composite Graph of Blood Pressure Recordings During the Operation

cated and differs according to various authors. Preoperative management may begin with 5-10 mg of regitine given intravenously in 5% glucose in water for 24 hours. This infusion is continued intraoperatively to minimize the risk of hypertensive crises and a solution of norepinephrine is prepared for immediate intravenous infusion if needed. Continuous monitoring of arterial and central venous pressure is carried out during the operation and fluid replacement is guided by these readings. Replacement with saline solution, plasma or whole blood begins with the skin incision and is dependent on the central venous pressure changes. Adequate replacement with fluids minimizes the amount of norepinephrine needed after removal of pheochromocytoma. Failure of the blood pressure to decrease to less than 120 millimeter pressure after removal of the tumor

indicates the presence of either residual tumor, functional metastasis or multiple pheochromocytomas. Cardiac arrhythmias are treated with xylocaine⁹.

Alternatively, preoperative management as proposed by other authors includes alpha adrenergic blocking agents for blood pressure greater than 200/130, with frequent severe uncontrolled hypertensive attacks and beta adrenergic blocking agents for a pulse faster than 140 per minute, history of any arrhythmia or pure epinephrine secreting tumors. When beta blocking agents are employed, alpha adrenergic blocking agents must be used. This combination avoids vasoconstriction unopposed by vasodilation and also decreases the load on the heart. Good preoperative preparation depends on adequate alpha adrenergic blockade. Dibenzyline is the drug of choice because regitine is too short acting for

adequate control. Unnecessary tests such as the regitine test, histamine test, or manipulations should be avoided¹⁴.

This patient was treated preoperatively with dibenzyline and propanolol and occasional doses of regitine. A central venous pressure catheter and arterial catheter were inserted for monitoring. The patient needed an extra dose of regitine during induction and during dissection of the adrenal gland. Vasopressor agents were not necessary to maintain a stable blood pressure after the adrenal gland was removed.

Recurrence of the symptoms following the removal of a pheochromocytoma may be due to inadequate resection of the primary tumor, failure to detect the presence of multiple pheochromocytomas, metastasis of an unrecognized malignant pheochromocytoma, the appearance of another primary tumor or to the development of essential hypertension. During the second exploration of this patient there was no evidence of metastasis to other organs. The time between the first operation and the recurrence of the symptoms probably indicates that the other adrenal gland is the site of another primary pheochromocytoma rather than a co-existing tumor present at the first operation.

The unexpected rise of the blood pressure after the second operation probably was due to essential hypertension and not to multiple pheochromocytomas or residual tumor because the blood pressure fell to 110 millimeters systolic pressure immediately following the removal of the adrenal gland. In addition, a repeat regitine test did not evoke a positive response. Furthermore, urinary catecholamines and metanephrines were within normal limits (table 1). Although the blood pressure returned to the preoperative levels, the patient's symptoms were alleviated.

PHEOCHROMOCYTOMA WITH ESSENTIAL HYPERTENSION

DOROMAL AND MIDDLETON

Hume had suggested subtotal adrenalectomy for the treatment of the second adrenal pheochromocytoma¹². This obviates the necessity of life-long steroid replacement. However, in large tumors, most of the adrenal gland is replaced by the tumor and a total adrenalectomy is necessary⁴. If a subtotal adrenalectomy were performed on the remaining adrenal gland of this patient, the recurrence of the hypertension would have strongly indicated an abdominal reexploration for residual pheochromocytoma.

References

1. LABBE, M., TINEL, J., DOUMER, A.: "Crises Solaires et Hypertension Paroxystique En Rapport Avec Une Tumeur Suprenale" *Bull. Soc. Med. Hop. Paris* 1922, 46:982.
2. MAYO, C. H.: "Paroxysmal Hypertension Associated with Tumor of Retroperitoneal Nerve" *J.A.M.A.* 1927, 89:1049.
3. RABIN, C. B.: "Chromaffin Cell Tumor of Suprarenal Medulla" *Arch. Path.* 1929, 7:228.
4. PAGE, L. B., COPELAND, R. B.: "Pheochromocytoma" *Disease a Month Jan.* 1968.
5. CROCKETT, K. A., SNOW, L., REES, V. L.: "Pheochromocytomas as Cause of Unexpected Operating Room Deaths" *Am. Surg.* 1969, 27:395.
6. BAKER, N. H., SWINDELL, H. F., ROLLINS, L. T.: "The Surgical Treatment of Bilateral Pheochromocytoma" *Ann. Surg.* 1964, 159:456.
7. COATES, P. A., RIGAL, W. M.: "Post-anesthetic Death from Pheochromocytoma without Hypertension" *Lancet* 1961, 1:1374.
8. GIFFORD, R. W., KVALE, W. F., MAHER, F. T., ROTH, G. M., PRIESTLY, J. T.: "Clinical Features, Diagnosis and Treatment of Pheochromocytoma: A Review of 76 Cases" *Mayo Clinic Proceedings*, 1964, 39: 281.
9. PERTSEMILIDES, D., GITLOW, S. E., SIEGAL, W. C., KARK, A. E.: "Pheochromocytoma: 1. Specificity of Laboratory Diagnostic Tests 2. Safeguards During Operative Removal" *Ann. Surg.* 1969, 169:376.
10. HARRISON, T. S., BARTLETT, J. D., SEATON, J. F.: "Current Evaluation and Management of Pheochromocytoma" *Ann. Surg.* 1968, 168:701.
11. GITLOW, S. E., PERTSEMILIDES, D., BERTANI, L.: "Management of Patients with Pheochromocytoma" *Amer. Heart Jour.* 1971, 82:557.
12. SCHWARTZ, S.: *Principles of Surgery* 1969, 1263.

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THE VIEW BOX

(from page 444)

An emergency Femoral Arteriogram was performed.



Fig. 1. PRE-OP



Fig. 2. POST-OP

The plain film shows a marked comminuted fracture of the distal tibia with depression of the lateral tibial plateau. The pre-operative Agniogram reveals almost complete occlusion of the popliteal artery. There are no collaterals. Immediate surgery demonstrated compression of the artery with laceration. Arterotomy was performed and clot removed.

Arterial injury in the form of laceration or vessel contusion is common after a fracture of the lower extremity. The distal femoral artery is frequently the site of injury because of its fixed position within the adductor canal. Displaced bone fragments may completely lacerate the artery with symptoms of acute arterial occlusion. Internal contusion, spasm and soft tissue bleeding may cause delayed ischemic changes. There are no contra-indications to Arteriography, even in shock. The exact location and type of vascular injury can be established.

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Isolated Agenesis of The Right Pulmonary Artery Terminating in Pneumonia in a Young Adult

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Abstract

A young Naval recruit with isolated agenesis of the right pulmonary artery, demonstrated ante mortem by lung scan, developed bilateral viral pneumonia predominantly involving the normal left lung with subsequent rapid deterioration in his clinical status as manifested by hypoxia and hypercapnia. Post mortem examination demonstrated a hypoplastic right lung and agenesis of the right pulmonary artery. Poor tolerance of pneumonia in these individuals as well as recommendations regarding environmental restrictions are discussed.

Introduction

Isolated agenesis of either the right or left pulmonary artery is an unusual finding. By 1962 Pool *et al.*¹ were able to collect 32 such cases from an extensive review of the world's literature. Reports have emphasized the frequent occurrence of pulmonary hypertension but have only mentioned pulmonary infection in passing. Reported is a young man with isolated agenesis of the right pulmonary artery who subsequently developed an extensive viral pneumonia predominantly affecting the normal left lung which

The potential problems which may arise in these patients (with isolated agenesis) when they develop pneumonia in the normally perfused lung was illustrated . . . As the pneumonia progressed in the lung the clinician was faced with a problem analogous to a bilateral pneumonectomy. Prevention and early vigorous treatment must be the guidelines . . .

lead to the patient's demise. Poor tolerance of pneumonia in these individuals as well as considerations regarding their environment are discussed.

Case History

A 19-year-old Navyman was admitted to the Naval Regional Medical Center, San Diego, because of a productive cough, fever and chills which developed while in boot camp. There was a history of recurrent pulmonary infections since birth. At age 17 years, a lung scan was performed which demonstrated absence of perfusion of

the right lung. The diagnosis of congenital absence of the right pulmonary artery was suspected.

Physical examination upon admission revealed a thin white man, with normal blood pressure, a resting pulse of 120 beats/minute, and an oral temperature of 102.3°F. The right chest was under-developed. There was decreased excursion of the right hemidiaphragm. Rales were present during auscultation of both bases, more markedly on the left.

The chest X-ray (Fig. 1) demonstrated dextroposition of the heart, tracheal deviation to the right, decreased right lung volume, and bibasilar pulmonary infiltrates, greater on the left than the right. The electrocardiogram demonstrated an S wave in lead V₁ measuring 27 mm.

The initial sputum examination was unremarkable. Erythromycin, 500 mg. q.i.d., which had been administered prior to admission due to the prevalence of mycoplasma infection in the recruit population was continued. Appropriate diagnostic studies failed to demonstrate a bacterial etiology for the pneumonia. By the third hospital day the infiltrate in the left lower lobe had progressed to include the lingula. At this point the patient was intubated

AGENESIS OF PULMONARY ARTERY WITH FATAL PNEUMONIA

VIEWEG, CONTE AND SCHILLACI



FIG. 1. Posterior-anterior roentgenogram of the chest demonstrating dextroposition of the heart, tracheal deviation to the right, decreased right lung volume, and bibasilar pulmonary infiltrates, greater on the left than the right.

because of progressive hypercapnia and hypoxemia. Despite appropriate measures including vigorous pulmonary toilet, tracheostomy, a trial of moderate dehydration and empiric antibiotic coverage the pneumonia progressed to opacification of both lung fields. On the tenth hospital day, the patient died.

At post mortem examination there was severe confluent acute bronchopneumonia, bilaterally. There was a hypoplastic right lung and agenesis of the right pulmonary artery (Fig. 2-A and 2-B). Intracardiac examination was entirely normal.

Discussion

Complaints of patients with isolated agenesis of the right or left pulmonary artery may include recurrent respiratory infections or hemoptysis. Rarely, pneumonectomy may be required for such problems when they occur repeatedly in the abnormal lung.² When infection involves the normal lung such an alternative is not possible since the abnormal lung cannot oxygenate the blood from the right heart.

The potential problems which may arise in these patients when they develop pneumonia in the normally perfused lung was dramatically illustrated in the present case. As the pneumonia progressed in the normal lung the clinician was faced with a problem analogous to a bilateral pneumonectomy. Prevention and early vigorous treatment must be the guidelines in such cases. Early recourse to membrane oxygenator support deserves serious consideration.

Placing such individuals in an environment conducive to the development of pneumonia such as a large dormitory or in boot camp is to be avoided. It should be noted that of 66 cases reported in the literature from 1950 to 1960, most were diagnosed ante mortem.¹ Patients with the diag-

nosis of unilateral pulmonary artery agenesis, and their families, should be thoroughly informed and advised of the need to avoid situations of high-risk with regard to additional pulmonary disability. These would include the use of tobacco, occupations involving exposure to significant levels of atmospheric contaminants, and military service.

References

1. POOL P. E., VOGEL J. H., BLOUNT S. G., JR.: Congenital unilateral absence of a pulmonary artery. *Am. J. Cardiol* 1962, 10:706-732.
2. MAIER H. C.: Absence or hypoplasia of a pulmonary artery with anomalous systemic arteries to the lung. *J. Thorac Cardiovasc Surg.* 1954, 28: 145-162.

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FIG. 2—A. Thoracic contents en bloc. Note hypoplasia of the right lung. The pulmonary artery supplied the left lung alone. There was a non-patent ductus arteriosus between the pulmonary artery and the aorta. FIG. 2—B. Close view of the normally related great vessels. The right pulmonary artery was absent. The pulmonary artery (PA) supplied the left lung alone. A non-patent ductus arteriosus (D) lay between the single pulmonary artery and the aorta (A).



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Supplied: **Tablets:** 0.025 mg., 0.05 mg., 0.1 mg., 0.15 mg., 0.2 mg., 0.3 mg., 0.5 mg., scored and color-coded in bottles of 100, 500, and 1000.

Injection: 500 mcg. lyophilized active ingredient and 10 mg. of Mannitol, U.S.P. in 10 ml. single-dose vial, with 5 ml. vial of Sodium Chloride Injection, U.S.P., as a diluent.

Synthroid-T₄



FLINT LABORATORIES

DIVISION OF TRAVENOL LABORATORIES, INC.

Deerfield, Illinois 60015



The Antacid Analogy



Indications: Pro-Banthine is effective as adjunctive therapy in the treatment of peptic ulcer. Dosage must be adjusted to the individual.

Contraindications: Glaucoma, obstructive disease of the gastrointestinal tract, obstructive uropathy, intestinal atony, toxic megacolon, hiatal hernia associated with reflux esophagitis, or unstable cardiovascular adjustment in acute hemorrhage.

Warnings: Patients with severe cardiac disease should be given this medication with caution.

Fever and possibly heat stroke may occur due to anhidrosis.

In the case of a severe like action may occur with loss of voluntary muscle

control. For such patients prompt and continuing artificial respiration should be applied until the drug effect has been exhausted.

Diarrhea in an ileostomy patient may indicate obstruction, and possibility should be considered before administering Pro-Banthine.

Precautions: Since varying degrees of urinary hesitancy may be evident by elderly males with prostatic hypertrophy, such patients should be advised to micturate at the time of taking the medication.

Overdosage should be avoided in patients severely ill with ulcer colitis.

Adverse Reactions: Varying degrees of drying of salivary secretions

Therapeutic comparisons in peptic ulcer.

Antacids have only one mode of action to relieve ulcer pain...

Pro-Banthine[®] has four modes of action of propantheline bromide

Antacids:

Antacids relieve ulcer pain by neutralizing gastric acid. This action is relatively short-lived and they have no other mode of action.

Pro-Banthine:

Pro-Banthine suppresses gastric acid secretion. The antisecretory properties of Pro-Banthine are well established. By effectively blocking vagotonic impulses Pro-Banthine suppresses gastric secretion to reduce both total and free acid.

Pro-Banthine helps relieve pain.

Pro-Banthine relieves ulcer pain by reducing gastric secretion and the motility and spasm of the gastrointestinal tract.

Pro-Banthine reduces acidity without subsequent acid rebound. The capacity of Pro-Banthine to reduce the secretion of total and free acid in the stomach has been demonstrated in scores of studies. None has demonstrated any significant evidence of acid rebound.

Pro-Banthine activity lasts about six hours. The effect of a single therapeutic dose (15 mg.) of Pro-Banthine lasts about six hours.* Pro-Banthine P.A.[®], the prolonged-acting form, is active from 8 to 12 hours. Thus Pro-Banthine may be used to suppress acid, spasm, and pain around the clock, even during the sleeping hours when antacids, to be effective, must be taken almost hourly.

*Innes, I. R., and Nickerson, M., in Goodman, L. S., and Gilman, A. (editors): The Pharmacological Basis of Therapeutics, ed. 4, New York, The Macmillan Company, 1970, p. 537.

Pro-Banthine complements and enhances the action of antacids.

SEARLE

Searle & Co.
San Juan, Puerto Rico 00936

Address medical inquiries to: G. D. Searle & Co.
Medical Department, Box 5110, Chicago, Ill. 60680

as well as mydriasis and blurred vision. In addition the following adverse reactions have been reported: nervousness, drowsiness, dizziness, insomnia, headache, loss of the sense of taste, nausea, vomiting, constipation, impotence and allergic dermatitis.

Dosage and Administration: The recommended daily dosage for adult therapy is one 15-mg. tablet with meals and two at bedtime. Subsequent adjustment to the patient's requirements and tolerance must be made.

Pro-Banthine P.A.—Each tablet of Pro-Banthine P.A. (propantheline bromide) contains 30 mg. of the drug in the form of sustained-release or

timed-release beads; on ingestion about half of the drug is released within an hour and the remainder continuously as earlier increments are metabolized. Thus the result is even, high-level anticholinergic activity maintained all day and all night in most patients with only two tablets daily. Some patients may require one tablet every eight hours.

The contraindications and precautions applicable to Pro-Banthine 15 mg. should be observed.

How Supplied: Pro-Banthine is supplied as tablets of 15 and 7.5 mg., as prolonged-acting tablets of 30 mg. and, for parenteral use, as serum-time vials of 30 mg.

The Role of the Detail Man

"I may be prejudiced, but I am very much in favor of the detail men I meet. Most of them are knowledgeable about the drugs they promote and can be a great help in acquainting me with new medication."

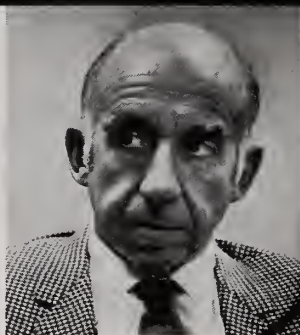
Family Physician's Perception

I think that most general practitioners in this area feel as I do about the detail man. Over the years I have gotten to know most of the men who visit me regularly and they in turn have become aware of my particular interests and the nature of my practice. They, therefore, limit their discussion as much as possible to the areas of interest to me. Since I usually see the same representative again in future visits, it is in his best interest to supply me with the most honest, factual, as well as up-to-date information about his products.

Dr. Willard Gobbell
Family Physician
Encino, California



Dr. Jeremiah Stamler
Chairman
Department of Community
Health and Preventive
Medicine, and Dingman
Professor of Cardiology
Northwestern University
Medical School



"In the total picture of dealing with health problems in this country, there is a potential for detail men to play a meaningful role."

The Positive Influence

My contact with representatives and salesmen of the pharmaceutical industry is the type of contact that people in a medical center, research people, and academic people have and that's in all likelihood on a somewhat different level from that of the practicing physician.

Let me touch on how I personally perceive the role of the sales representative. These men reach large numbers of health professionals. Thus they could be—and at times actually are—disseminators of useful information. They could consistently serve a real educational function in their ability to discuss their products.

At present they do distribute printed material, brochures and pamphlets—some of it scientifically sound and therefore truly useful—as well as some excellent films produced by the pharmaceutical industry. When they function in this

Opinion
&
Dialogue

Is He a Source of Information?

Yes, with certain reservations. The average sales representative has a great fund of information about the drug products he is responsible for. He is usually able to answer most questions fully and intelligently. He can also supply reprints of articles that contain a great deal of information. Here, too, I exercise some caution. I usually accept most of the statements and opinions that I find in the papers and studies which come from the larger teaching facilities. It goes without saying that a physician should also rely on other sources for his information on pharmacology.

Training of Sales Representatives

Ideally, a candidate for the position as a sales representative of a pharmaceutical company should be a graduate pharmacist who has a questioning mind. I don't think this is possible in every case, and so it becomes the responsibility

of the pharmaceutical company to train these individuals comprehensively. It is of very great importance that the detail man's knowledge of the product he represents be constantly reviewed as well as updated. This phase of the sales representative's education should be a major responsibility of the medical department of the pharmaceutical company.

I am certain that most of these companies take special care to give their detail men a great deal of information about the products they produce—information about indications, contraindications, side effects and precautions. Yet, although most of the detail men are well informed, some, unfortunately, are not. It might be helpful if sales representatives were reassessed every few years to determine whether or not they are able to fulfill their important function. Incidentally, I feel the same way about periodic assessments of everyone

in the health care field, whether they be general practitioners, surgeons or salesmen.

Value of Sampling

I personally am in favor of limited sampling. I do not use sampling in order to perform clinical testing of a drug. I feel that drug testing should rightly be left to the pharmacology researcher and to the large teaching institutions where such testing can be done in a controlled environment.

I do not use samples as a "starter dose" for my patients. I do, however, find samples of drugs to be of value in that they permit me to see what the particular medication looks like. I get to see the various forms of the particular medication at first hand, and if it is in a liquid form I take the time to taste it. In that way I am able to give my patients more complete information about the particular medications that I prescribe for them.

capacity they are indeed useful; particularly in the fact that they disseminate broadly based educational material and serve not just as "pushers" of their drugs.

The Other Side of the Coin

Obviously, the pharmaceutical companies are not producing all this material as a labor of love—they are in the business of selling products for profit. In this regard the ambitious and improperly motivated sales representative can exert a negative influence on the practicing physician, both by presenting a one-sided picture of his product, and by encouraging the practitioner to depend too heavily on drugs for his total therapy. In these ways, the salesman has often distorted objective reality and undermined his potential role as an educator.

The Industry Responsibility

Since the detail man must be an information resource as well as a representative of his particular pharmaceutical company, he should be carefully selected and

thoroughly trained. That training, perforce, must be an ongoing one. There must be a continuing battle within and with the pharmaceutical industry for high quality not only in the selection and training of its sales representatives, but also in the development of all of its promotional and educational material.

The industry must be ready to accept constructive as well as corrective criticism from experts in the field and consumer spokesmen, and be willing to accept independent peer review. The better educated and prepared the salesman is, the more medically accurate his materials, the better off the pharmaceutical industry, health professionals and the public—*i.e.*, the patients—will be.

Physician Responsibility

The practicing physician is in constant need of up-dated information on therapeutics, including drugs. He should and does make use of drug information and answers to specific questions supplied by the pharmaceutical representative. However, that informa-

tion must not be his main source of continuing education. The practitioner must keep up with what is current by making use of scientific journals, refresher courses, and information received at scientific meetings.

The practicing physician not only has the right, but has the responsibility to demand that the pharmaceutical company and its representatives supply a high level of valid and useful information. I feel certain that if such a high level is demanded by the physician as well as the public, this demand will be met by an alert and concerned pharmaceutical industry.

From my experience, my impression is that sectors of the pharmaceutical industry are indeed ethical. I challenge the industry as a whole to live up to that word in its finest sense.

Pharmaceutical
Manufacturers Association
1155 Fifteenth Street, N.W.
Washington, D. C. 20005



The more physicians consider the hemodynamics of lowering blood pressure...

Most physicians now agree on the importance of reducing blood pressure in the hypertensive patient. But high blood pressure exists, of course, only as part of a complete clinical picture. The hemodynamic profile of well-established essential hypertension is characterized by elevated arterial blood pressure, normal cardiac output, and increased total peripheral resistance.

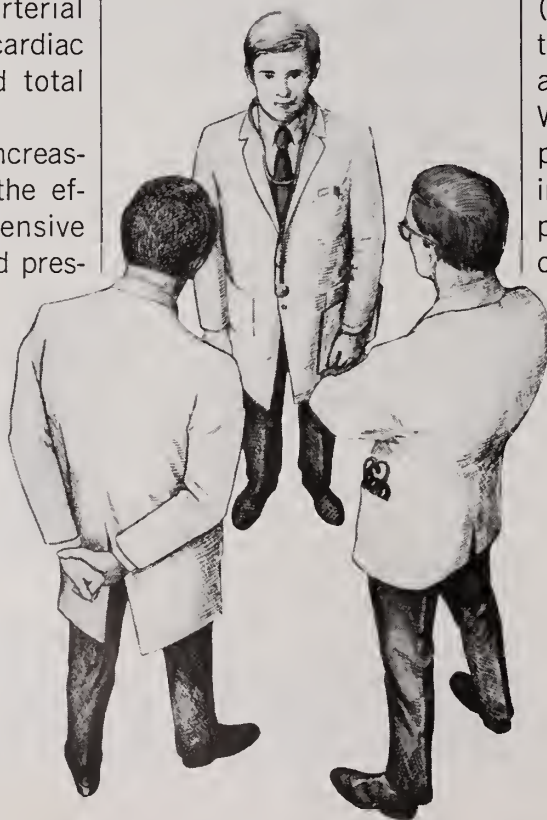
And so, physicians are increasingly concerned with the effects of an antihypertensive agent not only on blood pres-

sure itself but also on the hemodynamic pattern—in short, with the total effect of the drug. Does it indeed help lower blood pressure effectively? Is peripheral resistance reduced? Are cardiac output and renal functions main-

tained? And, also, is there likely to be drug-induced postural hypotension serious enough to pose a threat to the patient's cerebrovascular status?

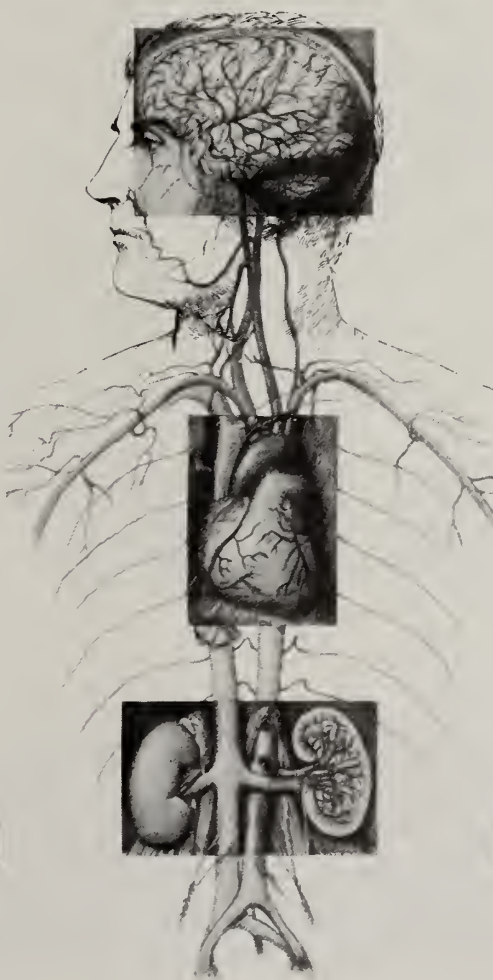
With this emphasis on overall drug performance has come a growing reliance on ALDOMET® (Methyldopa, MSD) in the treatment of sustained moderate hypertension.

With its unique hemodynamic profile, ALDOMET has drawn increasing attention and approval from physicians. First, of course, for its efficacy in



the more physicians rely on this unique antihypertensive

lowering blood pressure. But there are other considerations as well. Cardiac output is usually maintained with no cardiac acceleration; in some patients the heart rate is actually slowed. Peripheral resistance is apparently reduced. ALDOMET does not usually compromise existing renal function; it generally does not reduce renal blood flow, glomerular filtration rate, or filtration fraction. And ALDOMET usually does not cause symptomatic postural or exercise hypotension.



Contraindications include active hepatic disease and known sensitivity to the drug. Use with caution in patients with a history of liver disease or dysfunction. Not recommended in pheochromocytoma or pregnancy.

It is important to recognize that a positive Coombs test, hemolytic anemia, and liver disorders may occur with methyl dopa therapy. The rare occurrences of hemolytic anemia or liver disorders could lead to potentially fatal complications unless properly recognized and managed. For more details see the brief summary of prescribing information.

In most cases of sustained moderate hypertension

TABLETS, 250 mg and 500 mg

ALDOMET[®]

(METHYLDOPA | MSD)

smoothly lowers blood pressure

For a brief summary of prescribing information, please see following page.

NEW
now available in
500 mg TABLETS
as well as the standard
250-mg tablets

In most cases of
sustained moderate hypertension
ALDOMET[®]
(METHYLDOPA MSD)
smoothly lowers blood pressure

Contraindications: Active hepatic disease, such as acute hepatitis and active cirrhosis. Known sensitivity. Not recommended in pheochromocytoma. Unsuitable in mild or labile hypertension responsive to mild sedation or thiazide therapy. Use cautiously in patients with history of previous liver disease or dysfunction.

Warnings: It is important to recognize that a positive Coombs test, hemolytic anemia, and liver disorders may occur with methyldopa therapy. The rare occurrences of hemolytic anemia or liver disorders could lead to potentially fatal complications unless properly recognized and managed. Read this section carefully to understand these reactions.

With prolonged methyldopa therapy, 10% to 20% of patients develop a positive direct Coombs test, usually between six and twelve months of therapy. Lowest incidence is at daily dosage of 1 g or less. This on rare occasions may be associated with hemolytic anemia, which could lead to potentially fatal complications. One cannot predict which patients with a positive direct Coombs test may develop hemolytic anemia. Prior existence or development of a positive direct Coombs test is not in itself a contraindication to use of methyldopa. If a positive Coombs test develops during methyldopa therapy, determine whether hemolytic anemia exists and whether the positive Coombs test may be a problem. For example, in addition to a positive direct Coombs test there is less often a positive indirect Coombs test which may interfere with cross matching of blood.

At the start of methyldopa therapy, it is desirable to do a blood count (hematocrit, hemoglobin, or red cell count) for a baseline or to establish whether there is anemia. Periodic blood counts should be done during therapy to detect hemolytic anemia. It may be useful to do a direct Coombs test before therapy and at six and twelve months after the start of therapy. If Coombs-positive hemolytic anemia occurs, the cause may be methyldopa and the drug should be discontinued. Usually the anemia remits promptly. If not, corticosteroids may be given and other causes of anemia should be considered. If the hemolytic anemia is related to methyldopa, the drug should not be reinstituted. When methyldopa causes Coombs positivity alone or with hemolytic anemia, the red cell is usually coated with gamma globulin of the IgG (gamma G) class only. The positive Coombs test may not revert to normal until weeks to months after methyldopa is stopped.

Should the need for transfusion arise in a patient receiving methyldopa, both a direct and an indirect Coombs test should be performed on his blood. In the absence of hemolytic anemia, usually only the direct Coombs test will be positive. A positive direct Coombs test alone will not interfere with typing or cross matching. If the indirect Coombs test is also positive, problems may arise in the major cross match and the assistance of a hematologist or transfusion expert will be needed.

Fever has occurred within first three weeks of therapy, sometimes with eosinophilia or abnormalities in liver function tests, such as serum alkaline phosphatase, serum transaminases (SGOT, SGPT), bilirubin, cephalin cholesterol flocculation, prothrombin time, and bromsulphalein retention. Jaundice, with or without fever, may occur, with onset usually in the first two to three months of therapy. Rarely fatal hepatic necrosis has been reported. These hepatic changes may represent hypersensitivity reactions; periodic determination of hepatic function should be done particularly during the first six to twelve weeks of therapy or

whenever an unexplained fever occurs. If fever, abnormalities in liver function tests, or jaundice appear, stop therapy with methyldopa. If caused by methyldopa, the temperature and abnormalities in liver function characteristically have reverted to normal when the drug was discontinued. Methyldopa should not be reinstituted in such patients.

Rarely, reversible reduction in leukocyte count with primary effect on granulocytes has been seen. Reversible thrombocytopenia has occurred rarely. When used with other antihypertensive drugs, potentiation of antihypertensive effect may occur.

Use in Pregnancy and Childbearing Age—Not recommended in pregnancy. In women of childbearing age, weigh potential benefits against possible fetal hazards.

Precautions: Methyldopa may interfere with measurement of: uric acid by the phosphotungstate method, creatinine by the alkaline picrate method, and SGOT by colorimetric methods. Since methyldopa causes fluorescence in urine samples at the same wavelengths as catecholamines, spuriously high levels of urinary catecholamines may be reported. This will interfere with the diagnosis of pheochromocytoma. Stop drug if involuntary choreoathetotic movements occur in patients with severe bilateral cerebrovascular disease. Patients may require reduced doses of anesthetics; hypotension occurring during anesthesia usually can be controlled with vasopressors. Hypertension has occurred after dialysis in patients on methyldopa because the drug is removed by this procedure.

Adverse Reactions: Sedation, usually transient, may be seen during initial therapy or when dosage is increased. Headache, asthenia, or weakness may be noted as early, transient symptoms. Symptoms associated with effective lowering of blood pressure are occasionally seen and include dizziness, lightheadedness, and symptoms of cerebrovascular insufficiency. Angina pectoris may be aggravated. Symptoms of orthostatic hypotension may occur; if symptoms occur, reduction of dosage is suggested. Bradycardia, nasal stuffiness, mild dryness of mouth, and gastrointestinal symptoms including distention, constipation, flatulence, and diarrhea occur occasionally; these generally can be relieved by reducing dosage. Nausea and vomiting have been reported in only a few patients. Sore tongue or "black tongue," pancreatitis, and inflammation of salivary glands may occur.

Weight gain and edema occur infrequently and are relieved by administering a thiazide diuretic; if edema progresses or signs of pulmonary congestion appear, discontinue drug. A rise in BUN has been observed. Other rare reactions include breast enlargement, lactation, impotence, decreased libido, skin rash, mild arthralgia, myalgia, paresthesias, Bell's palsy, parkinsonism, psychic disturbances including nightmares, reversible mild psychoses or depression. Urine exposed to air after voiding may darken because of breakdown of methyldopa or its metabolites.

Note: Dosage should be limited initially to 500 mg daily when following previous antihypertensive agents other than thiazides. Maximal recommended daily dose is 3.0 g. Patients with impaired renal function may respond to smaller doses than patients with normal kidney function. Syncope in older patients has been related to increased sensitivity in those with advanced arteriosclerotic vascular disease; this may be avoided by lower doses. Tolerance occasionally seen either early or late, but more likely between second and third month after initiation of therapy; increased dosage or combined therapy with a thiazide frequently restores effective control.

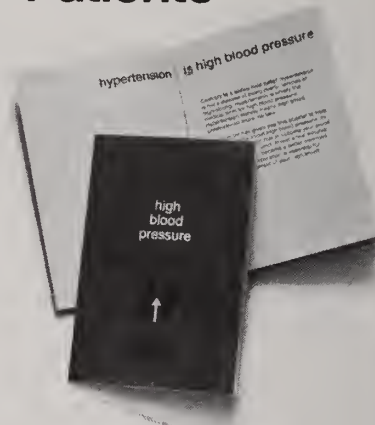
How Supplied: Tablets, containing 250 mg methyldopa each, in single-unit packages of 100 and bottles of 100 and 1000; Tablets, containing 500 mg methyldopa each, in single-unit packages of 100 and bottles of 100.

For more detailed information, consult your MSD representative or see full prescribing information. Merck Sharp & Dohme, Division of Merck & Co., Inc., West Point, Pa. 19486

MSD
MERCK
SHARP
DOHME

addendum

"Required Reading" For Your Hypertensive Patients



Because of the importance of patient motivation, Merck Sharp & Dohme offers "High Blood Pressure," a concise, pocket-sized booklet that defines the patient's own role in the management of hypertension. This booklet is available for you to give to your patients. It is designed to reinforce your explanation of hypertension and it emphasizes the importance of patient understanding in adhering to the regimen you prescribe.

Please ask your Merck Sharp & Dohme Professional Representative or write Professional Service Department, West Point, Pa. 19486 for a supply of this booklet.

COUGH



When a cough spoils your patient's day...

Triaminic® Expectorant

Each teaspoonful (5 ml.) contains:

Triaminic, 25 mg. (phenylpropanolamine hydrochloride, 12.5 mg.; pheniramine maleate, 6.25 mg.; pyrilamine maleate, 6.25 mg.); glyceryl guaiacolate, 100 mg.; alcohol, 5%.

Available in 8-oz. Family Size and 4-oz.

No Rx needed—recommend over the phone.

**The Adult Expectorant
that is great for kids, too.**

PRESCRIBING INFORMATION

Antiminth (pyrantel pamoate) Oral Suspension

Actions. Antiminth (pyrantel pamoate) has demonstrated anthelmintic activity against *Enterobius vermicularis* (pinworm) and *Ascaris lumbricoides* (roundworm). The anthelmintic action is probably due to the neuromuscular blocking property of the drug.

Antiminth is partially absorbed after an oral dose. Plasma levels of unchanged drug are low. Peak levels (0.05-0.13 µg/ml.) are reached in 1-3 hours. Quantities greater than 50% of administered drug are excreted in feces as the unchanged form, whereas only 7% or less of the dose is found in urine as the unchanged form of the drug and its metabolites.

Indications. For the treatment of ascariasis (roundworm infection) and enterobiasis (pinworm infection).

Warnings. *Usage in Pregnancy:* Reproduction studies have been performed in animals and there was no evidence of propensity for harm to the fetus. The relevance to the human is not known.

There is no experience in pregnant women who have received this drug.

Precautions. Minor transient elevations of SGOT have occurred in a small percentage of patients. Therefore, this drug should be used with caution in patients with pre-existing liver dysfunction.

Adverse Reactions. The most frequently encountered adverse reactions are related to the gastrointestinal system.

Gastrointestinal and hepatic reactions: anorexia, nausea, vomiting, gastralgia, abdominal cramps, diarrhea and tenesmus, transient elevation of SGOT.

CNS reactions: headache, dizziness, drowsiness, and insomnia. Skin reactions: rashes.

Dosage and Administration. *Children and Adults:* Antiminth Oral Suspension (50 mg. of pyrantel base/ml.) should be administered in a single dose of 11 mg. of pyrantel base per kg. of body weight (or 5 mg./lb.); maximum total dose 1 gram. This corresponds to a simplified dosage regimen of 1 cc. of Antiminth per 10 lb. of body weight. (One teaspoonful = 5 cc.)

Antiminth (pyrantel pamoate) Oral Suspension may be administered without regard to ingestion of food or time of day, and purging is not necessary prior to, during, or after therapy. It may be taken with milk or fruit juices.

How Supplied. Antiminth is available as a pleasant tasting caramel-flavored suspension which contains the equivalent of 50 mg. pyrantel base per ml., supplied in 60 cc. bottles and Unitcups™ of 5 cc. in packages of 12.

ROERIG 

A division of Pfizer Pharmaceuticals
New York, New York 10017

WORMS BLITZED



A single dose of Antiminth (1 cc. per 10 lbs. of body weight, 1 tsp./50 lbs. — maximum dose, 4 tsp.=20 cc.) offers highly effective control of *both* pinworms and roundworms.

Antiminth has been shown to be extremely well tolerated by children and adults alike in clinical studies.* Pleasantly caramel-flavored, it is non-staining to teeth and oral mucosa on ingestion... doesn't stain stools, linen or clothing.

One prescription can economically treat the entire family.

ROERIG **Pfizer**
A division of Pfizer Pharmaceuticals
New York, New York 10017

**Pinworms, roundworms controlled
with a single, non-staining dose of
ANTIMINTH[®]
(pyrantel pamoate)**

equivalent to 50 mg. pyrantel/ml.

ORAL SUSPENSION



Entrapped gas...

Silent partner of GI spasm

Painful GI spasm in the presence of entrapped gas causes even more pain and more discomfort. Yet, while spasm is relieved, entrapped gas often goes untreated.

Not so when you prescribe Sidonna. Sidonna helps release entrapped gas with specially activated simethicone, a nonsystemic antifatulent, while also helping to relieve spasm with a traditional combination of belladonna alkaloids. And Sidonna provides mild sedation with butabarbital.

Sidonna. The therapeutic partnership approach to functional or organic GI disturbances including spastic colon, irritable bowel syndrome, gastroenteritis, gastritis, peptic ulcer and nervous indigestion.

Contraindications: hypersensitivity to barbiturates or belladonna alkaloids; glaucoma, prostatic hypertrophy, pyloric obstruction. **Side Effects:** dry mouth, blurred vision, dysuria, skin rash, constipation or drowsiness. **Dosage:** one or two tablets preferably before meals and at bedtime.

Reed & Carnrick/Kenilworth, N.J. 07033 

Sidonna[®]

Each scored tablet contains: specially activated simethicone 25 mg., hyoscyamine sulfate 0.1037 mg., atropine sulfate 0.0194 mg., hyoscine hydrobromide 0.0065 mg. (equivalent to belladonna alkaloids [as bases] 0.1049 mg.) and butabarbital sodium N.F. 16 mg. (Warning: may be habit forming.)

**A working partnership
against the
pain of gas and spasm**



A half-ounce of prevention

Use it to prevent a topical infection. Or to treat one that's already started.

In either case, it's good medicine. Whether for lacerations, burns, open wounds, IV catheter or surgical aftercare.

Neosporin® Ointment provides broad antibacterial coverage against common susceptible pathogens. And since it contains three antibiotics that are rarely used systemically, the risk of sensitization is reduced.

Neosporin Ointment. A half-ounce of prevention. Also available in a full ounce of prevention and in convenient foil packets.

Neosporin Ointment carried on Apollo and Skylab missions.

Neosporin® Ointment (polymyxin B-bacitracin-neomycin)

Each gram contains: Aerosporin® brand Polymyxin B Sulfate 5,000 units; zinc bacitracin 400 units; neomycin sulfate 5 mg (equivalent to 3.5 mg neomycin base); special white petrolatum qs.
In tubes of 1 oz and 1/2 oz and 1/32 oz (approx.) foil packets.

INDICATIONS: Therapeutically, used as an adjunct to appropriate systemic therapy for topical infections, primary or secondary, due to susceptible organisms, as in: • infected burns, skin grafts, surgical incisions, otitis externa, primary pyodermas (impetigo, ecthyma, sycosis vulgaris, paronychia) • secondarily infected dermatoses (eczema, herpes, and seborrheic dermatitis) • traumatic lesions, inflamed or suppurating as a result of bacterial infection. Prophylactically, the ointment may be used to prevent bacterial contamination of burns, skin grafts, incisions, and other clean lesions. For abrasions, minor cuts and wounds accidentally incurred, its use may prevent the development of infection and permit wound healing.

CONTRAINDICATIONS: Not for use in the eyes or external ear canal if the eardrum is perforated. This product is contraindicated in those individuals who have known hypersensitivity to any of the components.

WARNING: Because of the potential hazard of nephrotoxicity and ototoxicity to neomycin, care should be exercised when using this product in treating extensive burns, trophic ulceration and other extensive conditions where

absorption of neomycin is possible. In burns where more than 20 percent of the body surface is affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended.

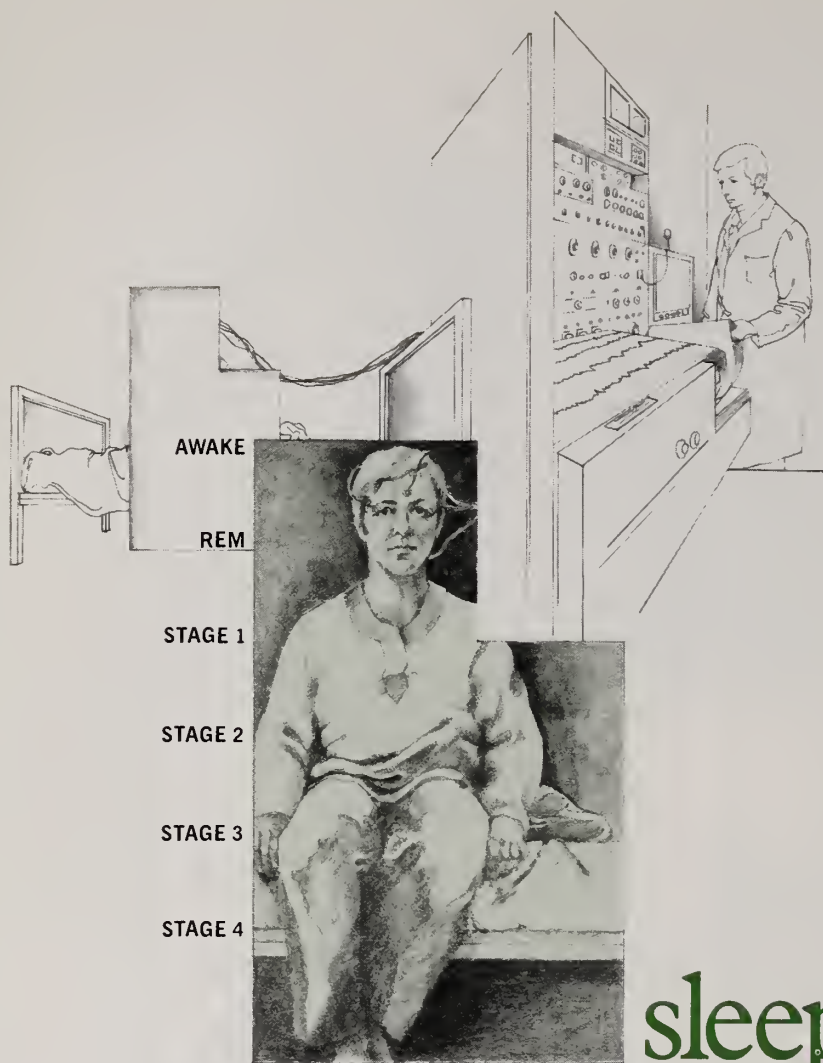
PRECAUTIONS: As with other antibacterial preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs.

ADVERSE REACTIONS: Neomycin is a not uncommon cutaneous sensitizer. Articles in the current literature indicate an increase in the prevalence of persons allergic to neomycin. Ototoxicity and nephrotoxicity have been reported (see Warning section).

Complete literature available on request from Professional Services Dept. PML.



Burroughs Wellcome Co.
Research Triangle Park
North Carolina 27709

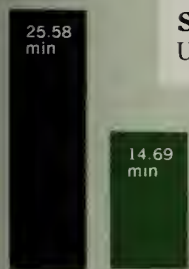


sleep
begins within
17 minutes, on average ...
an initial benefit of

Dalmane[®]
(flurazepam HCl) proved by a
22-night clinical study of insomnia patients
in the sleep research laboratory and at home¹

Three insomnia patients selected for difficulty falling asleep were administered Dalmane (flurazepam HCl) 30 mg for 14 consecutive nights. Placebo was given for four nights prior to and four nights after Dalmane. Physiologic tracings on Dalmane nights 1-3 showed sleep induction time averaged 13.90 minutes; on Dalmane nights 12-14, 18.80 minutes. Combined average for the 6 monitored drug nights was 16.35 minutes.¹

Average Time Required
to Fall Asleep (4 Studies,
16 Subjects²⁻⁵)



(Decreased 42.6%)

Baseline
(before Dalmane)

Dalmane
(flurazepam HCl) 30 mg

confirmed by clinical studies in four geographically separated sleep research laboratories²⁻⁵

Using a 14-night protocol involving eight insomniac and eight normal subjects, four studies confirmed the sleep-inducing effectiveness of Dalmane (flurazepam HCl) and the reproducibility of this response. On average, one 30-mg capsule induced sleep within 17 minutes. In all these studies, Dalmane induced sleep rapidly, reduced nighttime awakenings, and provided 7 to 8 hours of sleep without repeating dosage²⁻⁵

Dalmane (flurazepam HCl) induces and maintains sleep, with relative safety

Dalmane is generally well tolerated; morning "hang-over" has been relatively infrequent. While dizziness, drowsiness, lightheadedness and the like have been noted most often, particularly in the elderly and debilitated, physicians should be aware of the possibility of more serious reactions, as noted below.

Before prescribing Dalmane (flurazepam HCl), please consult Complete Product Information, a summary of which follows:

Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening; in patients with recurring insomnia or poor sleeping habits; and in acute or chronic medical situations requiring restful sleep. Since insomnia is often transient and intermittent, prolonged administration is generally not necessary or recommended.

Contraindications: Known hypersensitivity to flurazepam HCl.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Use in women who are or may become pregnant only when potential benefits have been weighed against possible hazards. Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated, initial dosage should be limited to 15 mg to preclude oversedation, dizziness and/or ataxia. If combined with other drugs having hypnotic or CNS-depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with latent depression or suicidal tendencies. Periodic blood counts and liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported were headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins and alkaline phosphatase. Paradoxical reactions, e.g., excitement, stimulation and hyperactivity, have also been reported in rare instances.

Dosage: Individualize for maximum beneficial effect. *Adults:* 30 mg usual dosage; 15 mg may suffice in some patients. *Elderly or debilitated patients:* 15 mg initially until response is determined.

Supplied: Capsules containing 15 mg or 30 mg flurazepam HCl.

REFERENCES: 1. Kales A, et al: *Arch Gen Psychiatry* 23:226-232, Sep 1970

2. Karacan I, Williams RL, Smith JR: The sleep laboratory in the investigation of sleep and sleep disturbances. Scientific exhibit at the 124th annual meeting of the American Psychiatric Association, Washington DC, May 3-7, 1971

3. Frost JD JR: Data on file, Medical Department, Hoffmann-La Roche Inc, Nutley NJ

4. Vogel GW: Data on file, Medical Department, Hoffmann-La Roche Inc, Nutley NJ

5. Dement WC: Data on file, Medical Department, Hoffmann-La Roche Inc, Nutley NJ



when restful sleep
is indicated

Dalmane[®] (flurazepam HCl)

One 30-mg capsule h.s. — usual adult dosage
(15 mg may suffice in some patients).

**One 15-mg capsule h.s. — initial dosage for
elderly or debilitated patients.**

- induces sleep within 17 minutes, on average
- reduces nighttime awakenings
- sustains sleep 7 to 8 hours, on average, without repeating dosage

ROCHE

ROCHE LABORATORIES
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110



What does man have in common with Samson?

Neither man nor the gorilla can synthesize vitamin C. Interestingly, the slow loris, a primate much further down the evolutionary scale, can convert L-1,4-gulonolactone to ascorbic acid in its liver and presumably does not require an exogenous source of ascorbic acid.

Because man can neither synthesize vitamin C nor store most of the water soluble vitamins, these nutrients must be replenished continuously in order to

maintain normal tissue levels.

Generally, this is accomplished in his daily diet. But under conditions of illness, stress, in convalescence or following surgery, vitamin stores may be depleted or metabolic demands increased.

In such cases, Surbex-T may be indicated. Surbex-T restores the water-soluble vitamins with each tablet providing 500 mg. of vitamin C plus high potency B-complex.



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Restores what the body cannot effectively store

The **ALLBEE**® with C Scrapbook of Vitamin Facts & Fallacies



The Indian fruit-eating bat, almost all monkeys, man and the guinea pig are the only mammals whose bodies lack an enzyme needed to synthesize ascorbic acid from glucose! Hence they must obtain their vitamin C from exogenous sources.

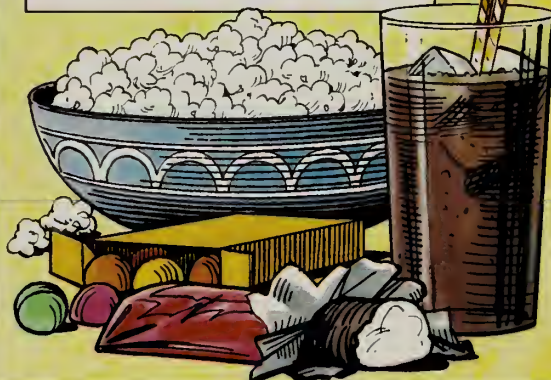


De Joinville writing about a 13th century crusade reported that barber surgeons had to "cut away the dead flesh from the gums to enable people to masticate their food." The disease he described was probably scurvy.



The outer leaves of cabbage and brussels sprouts contain more vitamin C than the heads. Yet, ironically, these are often trimmed away by the grocer to improve appearance and enhance sales appeal! Many housewives trim them even more before cooking!

A 1965 U.S.D.A. survey revealed that American diets were lower in vitamin C than they had been 10 years earlier!



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B-Complex and
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30 CAPSULES

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Spasm reactor?

Donnatal!

	each tablet, capsule or 5 cc. teaspoonful of elixir (23% alcohol)	each Donnatal No. 2	each Extentab
hyoscyamine sulfate	0.1037 mg.	0.1037 mg.	0.3111 mg.
atropine sulfate	0.0194 mg.	0.0194 mg.	0.0582 mg.
hyoscine hydrobromide	0.0065 mg.	0.0065 mg.	0.0195 mg.
phenobarbital	($\frac{1}{4}$ gr.) 16.2 mg.	($\frac{1}{2}$ gr.) 32.4 mg.	($\frac{3}{4}$ gr.) 48.6 mg.
(warning: may be habit forming)			

Brief summary. Adverse Reactions: Blurring of vision, dry mouth, difficult urination, and flushing or dryness of the skin may occur on higher dosage levels, rarely on usual dosage. Contraindications: Glaucoma; renal or hepatic disease; obstructive uropathy (for example, bladder neck obstruction due to prostatic hypertrophy); or hypersensitivity to any of the ingredients.

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*Based on surveys of average daily prescription costs.

Butisol  **SODIUM**
(SODIUM BUTABARBITAL)

Contraindications: Sensitivity or idiosyncrasy to barbiturates; history of manifest or latent porphyria or marked liver impairment; respiratory disease with dyspnea or obstruction; history of addiction to sedative/hypnotic drugs; uncontrolled pain, to avoid because of possible excitement.

Precautions: Exercise caution in: moderate to severe hepatic disease; anticoagulant therapy, because of possible increased metabolism of coumarin anticoagulants; withdrawal in drug dependence or the taking of excessive doses over a long period, to avoid withdrawal symptoms; elderly or debilitated patients, to avoid possible marked excitement or depression; use with alcohol or other CNS depressants, because of combined effects.

Adverse Reactions: Slight hangover, drowsiness, lethargy, headache, skin eruptions, nausea and vomiting, hypersensitivity reactions (especially in those with asthma, urticaria, angioneurotic edema, or similar conditions).

Usual Adult Dosage: For daytime sedation, 15 mg. to 30 mg. t.i.d. or q.i.d. For hypnosis, 50 mg. to 100 mg.

Available as: Tablets, 15 mg., 30 mg., 50 mg., 100 mg.; Elixir, 30 mg. per 5 cc. (alcohol 7%). BUTICAPS® [Capsules BUTISOL SODIUM (sodium butabarbital)] 15 mg., 30 mg., 50 mg., 100 mg.

McNEIL

Neil Laboratories, Inc., Fort Washington, Pa. 19034

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What's on your patient's face...

may be more important than his chief complaint

Patient P.T.* seen on 3/29/67 shows typical lesions of moderately severe keratoses. Note residual scarring on ridge of nose from previous cryosurgical and electrosurgical procedures.



Patient P.T.* seen on 6/12/67, seven weeks after discontinuation of 5% FU cream. Reaction has subsided. Residual scarring not seen except that due to prior surgery. Inflammation has cleared and face is clear of keratotic lesions.

*Data on file,
Hoffmann-La Roche
Inc., Nutley, N.J



The lesions on his face are solar/actinic—so-called “senile” keratoses... and they may be premalignant.

Solar, actinic or senile keratoses

These lesions may be called by several names, but they usually can be identified by the following characteristics. The typical lesion is flat or slightly elevated, of a brownish or reddish color, papular, dry, rough, adherent and sharply defined. They commonly occur as multiple lesions, chiefly on the exposed portions of the skin.

Sequence of therapy—selectivity of response

After several days of therapy with Efudex® (fluorouracil), erythema may begin to appear in the area of the lesions; this reaction usually reaches its height of unsightliness and discomfort within two weeks, declining after discontinuation of therapy. This reaction occurs in affected areas. Since the response is so predictable, lesions that do not respond should be biopsied.

Acceptable results

Treatment with Efudex provides highly favorable cosmetic results. Incidence of scarring is low. This is particularly important with multiple facial lesions. Efudex should be applied with care near the eyes, nose and mouth.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Multiple actinic or solar keratoses.

Contraindications: Patients with known hypersensitivity to any of its components.

Warnings: If occlusive dressing used, may increase inflammatory reactions in adjacent normal skin. Avoid prolonged exposure to ultraviolet rays. Safe use in pregnancy not established.

Precautions: If applied with fingers, wash hands immediately. Apply with care near eyes, nose and mouth. Lesions failing to respond or recurring should be biopsied.

Adverse Reactions: Local—pain, pruritus, hyperpigmentation and burning at application site most frequent; also dermatitis, scarring, soreness and tenderness. Also reported—insomnia, stomatitis, suppuration, scaling, swelling, irritability, medicinal taste, photosensitivity, lacrimation, leukocytosis, thrombocytopenia, toxic granulation and eosinophilia.

Dosage and Administration: Apply sufficient quantity to cover lesion twice daily with nonmetal applicator or suitable glove. Usual duration of therapy is 2 to 4 weeks.

How Supplied: Solution, 10-ml drop dispensers—containing 2% or 5% fluorouracil on a weight/weight basis, compounded with propylene glycol, tris(hydroxymethyl)aminomethane, hydroxypropyl cellulose, parabens (methyl and propyl) and disodium edetate.

Cream, 25-Gm tubes—containing 5% fluorouracil in a vanishing cream base consisting of white petrolatum, stearyl alcohol, propylene glycol, polysorbate 60 and parabens (methyl and propyl).



Roche Laboratories
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Nutley, N.J. 07110

This patient's lesions were resolved with

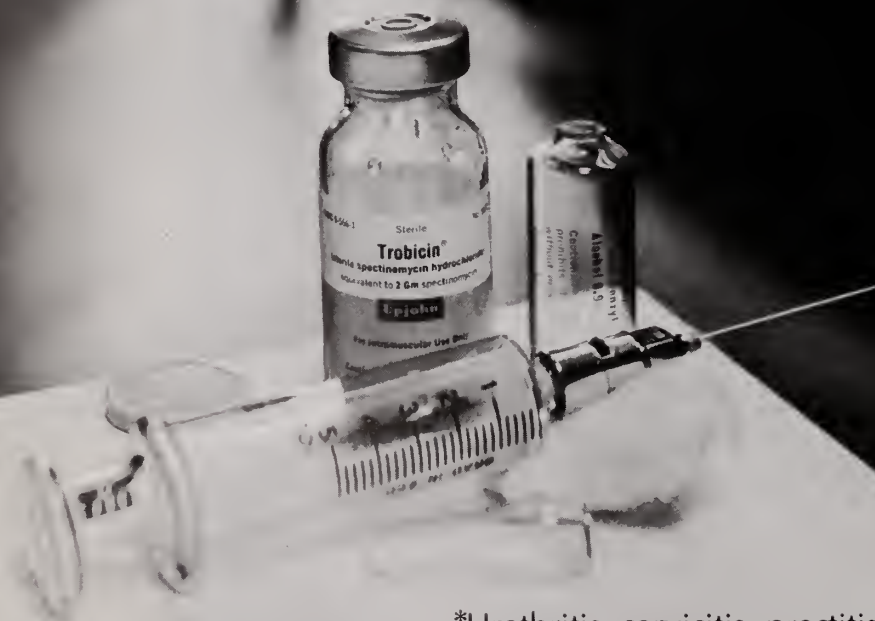
Efudex® fluorouracil/Roche®

5% cream/solution...a Roche exclusive

acute gonorrhea

This patient
just received
an effective, private,
physician-controlled
treatment.

It took just one short visit..



*Urethritis, cervicitis, proctitis when due
to susceptible strains of *N. gonorrhoeae*

Trobicin—The advantage of injectable therapy.

Once Trobicin is injected, treatment is usually complete; there can be no problems with patients sharing, skimping, skipping or forgetting medication.

Trobicin—The aspect of privacy.

There are no prescriptions to fill, no capsules to take. Neither family, friends nor co-workers need know or suspect the patient's problem.

Trobicin—Indication and dosage.

Spectinomycin is indicated only for use in acute urethritis and proctitis in the male and acute cervicitis and/or proctitis in the female when due to susceptible strains of *N. gonorrhoeae*. The usual dosage for Trobicin in adult males is 2 grams intramuscularly[†]; 4 grams intramuscularly in females.

Trobicin—Not effective for syphilis.

Trobicin is not effective for any stage of syphilis. Trobicin may mask or delay the symptoms of incubating syphilis. If concurrent syphilis is suspected, follow the patient serologically for at least 3 months. Patients with syphilis should receive adequate specific anti-syphilitic therapy with an appropriate antibiotic. Trobicin is contraindicated in patients previously found hypersensitive to it.

Intramuscular

...and **Trobicin**[®] 2 gm and 4 gm vials sterile spectinomycin hydrochloride

Sterile Trobicin

Sterile Trobicin (spectinomycin hydrochloride)
— For Intramuscular Injection:

2 gm vials containing 5 ml when reconstituted with diluent.

4 gm vials containing 10 ml when reconstituted with diluent.

An aminocyclitol antibiotic active *in vitro* against most strains of *Neisseria gonorrhoeae* (MIC 7.5 to 20 mcg/ml). Definitive *in vitro* studies have shown no cross resistance of *N. gonorrhoeae* between spectinomycin and penicillin.

Indications: Acute gonorrheal urethritis and proctitis in the male and acute gonorrheal cervicitis and proctitis in the female when due to susceptible strains of *N. gonorrhoeae*.

Contraindications: Contraindicated in patients previously found hypersensitive to spectinomycin.

Warnings: Not indicated for the treatment of syphilis. Antibiotics used to treat gonorrhea may mask or delay the symptoms of incubating syphilis. Patients should be carefully examined and monthly serological follow-up for at least 3 months should be instituted if the diagnosis of

syphilis is suspected.

Safety for use in infants, children and pregnant women has not been established.

Precautions: The usual precautions should be observed with atopic individuals. Clinical effectiveness should be monitored to detect evidence of development of resistance by *N. gonorrhoeae*.

Adverse reactions: The following reactions were observed during the single-dose clinical trials: soreness at the injection site, urticaria, dizziness, nausea, chills, fever and insomnia. During multiple-dose subchronic tolerance studies in normal human volunteers, the following were noted: a decrease in hemoglobin, hematocrit and creatinine clearance; elevation of alkaline phosphatase, BUN and SGPT. In single- and multiple-dose studies in normal volunteers, a reduction in urine output was noted. Extensive renal function studies demonstrated no consistent changes indicative of renal toxicity.

Dosage and administration: Keep at 25° C and use within 24 hours after reconstitution with diluent.

Male—Inject 5 ml intramuscularly for a 2 gram dose. Patients with gonorrheal proctitis and patients being re-treated after failure of previous antibiotic therapy should receive 4 grams (10 ml). In geographic areas where antibiotic resistance is known to be prevalent, initial treatment with 4 grams (10 ml) intramuscularly is preferred.

Female—Inject 10 ml intramuscularly for a 4 gram dose.

How supplied: Vials, 2 and 4 grams—with ampoule of Bacteriostatic Water for Injection with Benzyl Alcohol 0.9% w/v. Reconstitution yields 5 and 10 ml respectively with a concentration of 400 mg spectinomycin per ml (as the hydrochloride). For intramuscular use only. **Susceptibility Powder**—for testing *in vitro* susceptibility of *N. gonorrhoeae*.

Caution: Federal law prohibits dispensing without prescription.

For additional product information see your Upjohn representative or consult the package insert.

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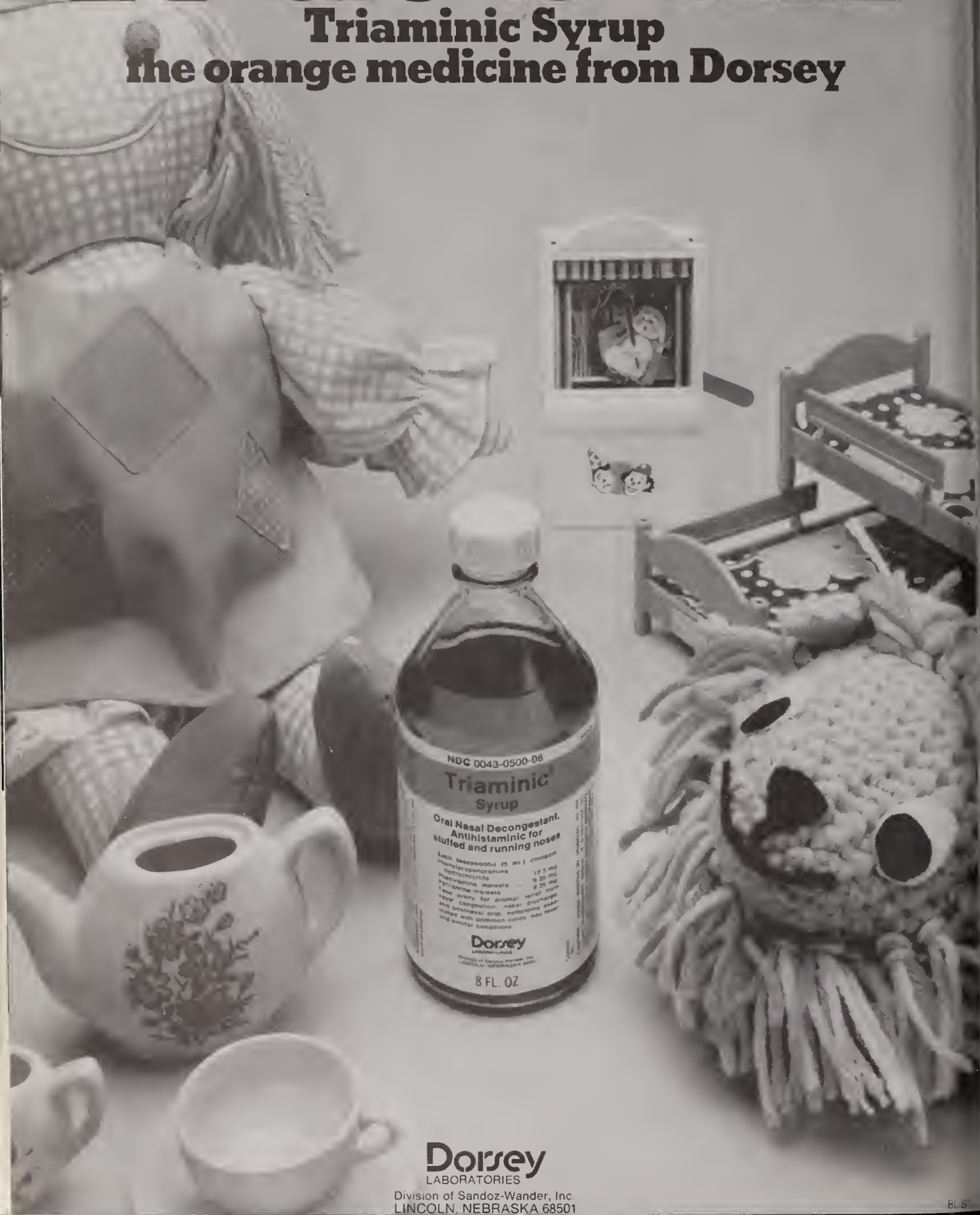
The Upjohn Company, Kalamazoo, Michigan 49001

MED 8-5-S (MBR-1)

[†]For patients with gonorrheal proctitis and for patients in geographic areas where antibiotic resistance is known to be prevalent, initial treatment with 4 grams is preferred.

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the orange medicine from Dorsey



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BL 57

BOOK REVIEWS

Before Addiction: How to Help Youth.

FLORENCE LIEBERMAN, PHYLLIS CAROFF
AND MARY GOTTESFELD. Price, \$7.95. Pp. 131.
New York: Behavioral Publications, 1973.

This book on drug use is written for the layman and advice is offered to help parents and the adolescent who need guidance in preventing the use of drugs and possible subsequent addiction.

The authors of the book make a distinction in dealing with the drug problem of adolescents stressing considerations to those drug users before drug abuse and/or addiction, the use of various drugs that may be dangerous for growing bodies and minds.

The young person, anxious and fearful, who may manifest physical and psychological dependence, who has not learned to tolerate frustrations and tensions, is vulnerable to drug addiction. Such individuals may have social, intellectual and personality conflicts. Help must be given to these people before they turn to drugs in coping with life problems.

Factors of environmental influences, the peer group and involvement of home conditions are considered. Although among parents being old fashioned is currently unpopular, a trusting relationship between parent and offspring is necessary to his learning how to be an adult. Discipline and a definite stand must be taken on any drug as it will be easier to deal with prohibiting drug use by young people than contradictions, confusion and inconsistency by the parents. Moreover, both parents must cooperate and be in agreement on issues.

It is most important knowing your child in relation to how he has been and how he is. Parents who notice any unexplainable changes in their adolescent's behavior, ie. emotional disturbances, depression, academic and activity failures need to consider drug use as a possible reason.

For the adolescent, he should have the opportunity to speak to an adult, whether the parent, relative, close friend or teacher. (One must be honestly interested in the adolescent in their endeavor to help and communicate with the youngster.) Whenever therapy, psychotherapy, professional or other types are instituted, under no circumstances should the parent be excluded. The authors feel that confrontation "experts" who have been former addicts may not be good therapists.

This book is worthwhile reading for better insight in the drug problem concerning youth of all levels of society and there are many suggestions for those concerned with and involved in such situations.

JOHN G. STUBENBORD, M.D.

CORNEAL GRAFT FAILURE. Edited by B.R. Jones. Ciba Foundation Symposium. Elsevier Associative Scientific Publications, Amsterdam, London, New York. 363 pages. 1973.

This excellent volume is, in effect, the proceedings of a Ciba Foundation-sponsored symposium held in late 1972 in London. Twenty-two participants present papers in well-defined areas related to their special interests; each paper is followed by a round table discussion. Of the eighteen papers, fourteen are devoted to corneal graft rejection (allograft reactions). This represents a disproportionate emphasis on what is certainly not the principal cause of graft failures, but reflects the intense interest and recent research findings in this fascinating area.

Graft failure, i.e., the failure of a grafted donor corneal button to maintain its clarity, needs to be put in perspective. Advances in instrumentation, technique and the understanding of corneal pathophysiology and its management have led to a greatly improved prognosis in keratoplasty. Successful results can be anticipated in 65 to 90% of reasonably favorable prognostic categories a few diseases are still associated with poor prognosis, e.g., severe chemical burns, Stevens-Johnson disease, ocular pemphigoid, because of a variety of problems encountered, i.e., the release of collagen-digesting enzymes, desiccation of the corneal surface and impaired epithelial healing. Even in the more favorable prognostic groups, successful results are not routine. In these groups, most grafts that fail do so because of endothelial failure secondary to surgical trauma, adhesions or (and more importantly), unhealthy donor endothelium without enough functional reserve to withstand the insult of transplantation. We really lack a reliable method of assessing the functional status of donor endothelium prior to transplantation. Of particular promise is a newly reported biomicroscope using specular reflection to visually assess endothelial cell morphology.

It has been estimated that bonafide graft rejection occurs in about 11-13% of corneal grafts. This is a significant figure; on the other hand it is true that diagnosed early and treated vigorously with corticosteroids, these inflammatory reactions can usually be reversed before severe, irreversible structural damage is done. Recognition and adequate treatment are the keynotes.

Three of the participants have contributed greatly to our knowledge of the basic mechanisms involved in graft rejections. The papers by Khondadoust, Silverstein and Polack are excellent summaries of the

BOOK REVIEWS

present state of knowledge and the superb scanning electron photomicrographs of Polack are striking. It has been shown that endothelium, stroma and epithelium can be rejected separately. Clinically, endothelial rejection is most important and the recognition of an endothelial rejection line (Khodadoust) as a pathognomic sign of rejection has been a great help in defining criteria for the diagnosis of a graft rejection. These criteria, well-defined in the book, should be studied by corneal surgeons, many of whom have previously attributed all graft failures to rejection.

Also contained in this book are timely discussions of the problems attendant on corneal grafting in herpetic keratitis and the difficulty distinguishing return of stromal keratitis from graft rejection. Perhaps the most fascinating part of the book is the dialogue of well-informed surgeon researchers narrowing and defining critical questions to be answered in the field of corneal grafts, e.g., the pros and cons of retaining donor epithelium.

Not the least of the book's attributes is the Chairman, Professor Jones' succinct expression of the clinical state of the art and identification of problems that remain unanswered. This book should be read by all attempting corneal surgery; it fills a critical need.
MICHAEL A. LEMP, M.D.

Look for the Monthly Issue of the MEDICAL SOCIETY OF D.C. NEWS

***Society's news, activities
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The habit called heroin.



In East Harlem, the AMA helped a lot of addicts kick it.

Where can I get help? What will happen to me? Will I be arrested? Who can I trust? For an addict, the answers are often critical to his decision to seek help.

In East Harlem, he knows where he can get the right answer and help: the Drug Referral Agency right in his community. It's staffed by former addicts who are intimately familiar with an addict's needs. Since opening its door, the agency has helped hundreds of addicts kick the habit.

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MANUSCRIPT

The entire manuscript, including footnotes and case reports, should be submitted unrolled, with double type spacing. An original copy and one carbon copy should be submitted, and a carbon copy should be retained by the author.

The title should not exceed 80 characters and spaces. If a subtitle is used, it should not be connected grammatically to the main title.

The by-line, the author's given name and initial or given name alone should be supplied. The M.D. degree or highest academic degree should be listed for each author. Not more than six names should be included as authors, unless the communication is the report of a committee.

The footnotes, hospital and university affiliation when study was done, should be listed. Present affiliation and location (if different from that at time of study) should be given. Acknowledgements should be limited to persons, foundations, agencies or companies supplying drugs, funds or apparatus free of charge or otherwise making an extensive contribution to the study.

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References should be given in the style regularly used in THE ANNALS, eg:

Seremetis, M.D., DeGuzman, V.C.,
Lyons, W.S., Peabody, J.W.: Complications of Cardiac Pacemakers, Medical Annals of D.C., 1973, 42, 165.

TEXT

Use generic or descriptive names of drugs when available. Trade names, capitalized, may be given in parentheses when the drug is first mentioned.

Statistics should be checked for consistency within the text and for agreement with graphs or tables.

Laboratory data should not be given in abbreviated form but in full (e.g., "hemoglobin level, 12 Gm. per 100 ml." rather than "Hb. 12 GM.%).

Figures should be used for number 10 and above, laboratory measurements, percentages, and ages.

Metric equivalents should be given for dosage and body height and weight.

Centigrade equivalents should be given for Fahrenheit body temperatures, and vice versa.

Abbreviations should be used sparingly, with expansion given for those not listed in standard medical dictionaries.

The meaning of "we" should be clarified, especially if there is only one author. Avoid use of editorial "we."

SUBHEADINGS

One center heading should be supplied for about every three pages of double-spaced text copy. Subdivisions of main topics should be indicated by side headings.

SUMMARY

The summary should be brief, giving specific facts concerning the study and its results.

ADDRESS

The street address of one author should be given at the end of the article for reprint requests and correspondence.

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The title should be given at top of the page for each table.

Approximate placing of tables in text should be indicated, and each table should be referred to in the text.

The meaning of abbreviations should be clear, with those not listed in standard medical dictionaries expanded in a footnote to the table.

There should be no discrepancies in the totals.

Figures should be consistent with the text, without extensive duplication between tables and text or graphs.

All material under each column heading should be parallel in meaning.

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Simple tabular material should be incorporated into the text in sentence form.

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Only necessary illustrations should be submitted.

Photographs should be submitted as unmounted black-and-white glossy prints.

Graphs and line drawings should be prepared with black india ink on white paper, with uniform lettering which will be legible when the illustration is reduced to 3-1/8-in. in width.

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Permission should be received and credit given in legend or footnote for use of illustrations published elsewhere.

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Arrows should be inserted to pinpoint lesion or any important feature.

Do not attach paper clips or cellophane tape to photographs.

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A synopsis-abstract not to exceed 150 words must accompany the manuscript.

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INDEX TO ADVERTISERS

Equipment and Supplies

Kloman Surgical Supply Co. 2

Insurance

Corroon & Black, Russell, Inc. 6

Ralph W. Lee & Company T-460

Mutual of Omaha 4

Nurse Registries

District of Columbia Manpower

Administration 490

Nutrition Education

Dairy Council of greater Metropolitan

Washington, D.C. 2

Pharmaceuticals

Abbott Laboratories-476

Burroughs Wellcome & Company T-473

Dorsey Laboratories T-469, T-484

Flint Laboratories T-461

Eli Lilly & Company 8

McNeil Laboratories T-479

Merck, Sharp & Dohme Laboratories . T-466-468

Pharmaceutical Manufacturers Association .T-464

Reed & Carnrick T-472

A.H. Robins Company T-4 77, 478

Roche Laboratories C2, 1, C3, C4

J.B. Roerig 470-471

G.D. Searle & Company 462

Upjohn Company 482-483

Pharmacy

Peoples Drug Stores 7

Therapy

The University Center 489

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For further information on this subject, the following references are provided:

1. Henry BW, *et al: Dis Nerv Syst* 30:675-679, Oct 1969.
2. Hollister LE, *et al: Arch Gen Psychiatry* 24:273-278, Mar 1971.
3. Claghorn J: *Psychosomatics* 11:438-441, Sept-Oct 1970.

surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of child-bearing age, weigh potential benefit against possible hazard.

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CONTENTS

SCIENTIFIC ARTICLES

The Frequency and Fate of Pregnancy After Age 45. David H. Kushner, M.D.	491
Premature Menopause: A Report of Two Cases. Richard J. Falk, M.D.	493
Mixed Mesodermal Tumors of the Corpus Uteri. William J. Jaffurs, M.D., Douglas G. Martz, M.D., Steele Stewart, M.D. and J. Keith Cromer, M.D.	497
Leiomyomata with Aplasia of the Uterus and Fallopian Tubes: A Case Report. J. Keith Cromer, M.D., William J. Jaffurs, M.D. and Douglas G. Martz, M.D.	499
Colposcopic Evaluation of Stilbestrol Exposed Young Women. John L. Marlow, M.D.	503

OTHER FEATURES

Editorial	5
Embryo Transplant—Worthy Goal or Mis-Conception. Richard J. Falk, M.D.	
The View Box	496
Edited by Gunther J. Augustin, M.D.	
ECG Problems	502
Edited by Robert R. Montgomery, M.D.	
Book Reviews	525
Patterns in Forcible Rape. (Amir) Reviewed by Edward H. Weiss, M.D.	
Ureteral Dynamics, Pathophysiology, Drugs, and Surgical Implications. (Boyarsky and Labay) Reviewed by Hector H. Herrera, M.D.	
Information for Authors	530
Advertising and Subscription Information	532
Index to Advertisers	532

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Editorial

Recently a spectacular (and irregular) announcement focused public attention on an extremely controversial medical topic, "test tube babies" (more properly, embryo transplant). The announcement, made to the general public without scientific documentation, was that three children who were the product of *in vitro* fertilization with subsequent intrauterine implantation of the early embryo were alive and normal in Europe. Blistering criticism followed from almost all quarters against the purported investigator, his method of releasing the results, and against the procedure in general.

Stepoe and Edwards are generally considered to be the pioneers in this emotionally charged area. They were the first to aspirate ova through the laparoscope from women stimulated with exogenous gonadotrophins, and fertilize them *in vitro*. In a culture medium a small percentage of these embryos can be maintained until they reach the blastocyst stage which is when, under normal conditions, implantation occurs. Implantation of cultured blastocysts has been reported several times in lower animals, with resulting normal offspring, but had not been reportedly successful in humans despite numerous attempts until the above mentioned announcement. The lack of data acceptable to the scientific community, however, renders this claim anecdotal.

The condemnations of human embryo transplant take several tacks. One argument is that the procedure constitutes or will lead to genetic tampering. Because many of the investigators are

embryologists and geneticists, their experiments in lower animals have involved not only transfer but manipulation of genetic material. In cloning, for instance, the nucleus of a cell is substituted for the nucleus of an unfertilized egg, resulting in an embryo that is genetically identical to the donor. This has been successful in lower animals, and has frightening implications for humans. It evokes clearly Huxley's "Brave New World" with its homogeneous classes of test tube humans. But cloning has not been performed in humans, nor have the advocates of human embryo transfer as a potential clinical tool suggested that cloning is the next step.

Kass declared that "infertility . . . is not a disease, so providing a child by artificial means to a woman with blocked oviducts is not treatment (as surgical reconstruction of her oviducts would be)." Infertility is not a disease but a symptom. Tubal obstruction, however, is a disease, and surgical reconstruction has a rather poor success rate. This fact, along with the increasing incidence of tubal disease and the decreased availability of babies for adoption, make a tubal bypass procedure desirable. Medicine is replete with examples of bypass or substitution procedures when the original function is irrevocably lost. Is insulin a *cure* for diabetes mellitus? Does a coronary artery bypass *cure* arteriosclerotic coronary artery disease? Do, in fact, corrective lenses *cure* myopia or astigmatism? We must point out that the artificial maintenance of such defective individuals is contaminating the genetic pool of our species. To go even further, any societal aid that tends to "thwart"

the "survival of the fittest" theory might be equally condemned. Yet we certainly do not condemn such modalities, but rather support them, and, I think, rightly so.

I consider the argument that human embryo transplant is wrong because it entails experimentation and manipulation of potential and early human organisms to be the most valid objection. It must be conceded that in embryo transplant, as in many other human manipulations, the risks are not completely known. There have been no reports of gross deformities at birth of transplanted embryos in lower animals. It is generally accepted that damage to an ovum before organogenesis is usually lethal to the embryo; that is, specific organ defects occur during the development of that organ. The manipulations involved in embryo transplant take place before organogenesis, which under these circumstances would occur after nidation, when the embryo is in its "natural" place of development. It would appear, therefore, that embryo transplant would be an "all-or-nothing" phenomenon to the embryo. It either implants and develops normally in a natural environment, or is destroyed by the manipulation or failure to implant.

Is the blastocyst a human? This point has been discussed and re-worked again and again in relation to

the abortion topic. Contraceptive devices (IUD's), which alter the endometrial environment so the blastocyst cannot implant (or is damaged), are taken for granted by most.

The abortion debate continues, over a procedure which entails the *deliberate* destruction of an embryo or fetus. Surely the loss of an embryo during an attempt at implantation is more akin to the occurrence of an ectopic pregnancy following tuboplasty.

The research on tubal bypass should, I feel, continue both in lower animals and humans, with the ultimate goal of aiding those victims of incurable obstructive tubal disease to achieve what is a vital function in any living species—reproduction.

R. J. Falk, M.D.

Chief, Reproduction Research Unit

Columbia Hospital for Women

Clinical Assistant Professor

Department of Obstetrics and Gynecology

George Washington University Hospital

References

1. Edwards, R. E., Steptoe, P. C., Purdy, J. M., *Nature*, London 227:1307, 1970.
2. Kass, L. R., *N.E.J.M.* 285:1174-1179, 1971.

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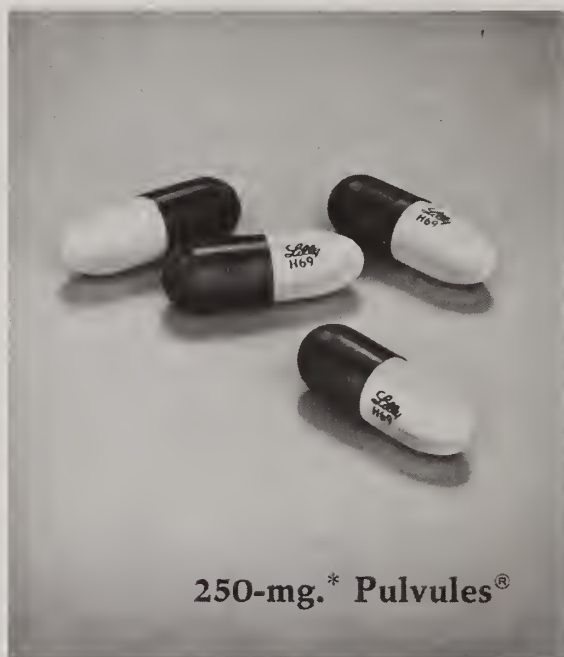
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SCIENTIFIC ARTICLES

The Frequency and Fate of Pregnancy After Age 45

DAVID H. KUSHNER, M.D., F.A.C.S., F.A.C.O.G.

Abstract

The frequency and fate of pregnancy after age 45 is discussed. An analysis was made for the six year period from June 1967 to December 1972 at Columbia Hospital for Women in Washington, D.C. There were 28,796 deliveries with nine patients in the 45-48 age group. The oldest mother with a viable baby was 48 years old. There were 11,057 abortions, of which 40 occurred in patients over age 45; eighteen were induced and 22 were spontaneous. There were 5 hydatidiform moles, including one in the oldest patient who was 51. A comparison of our statistics with those of 5 large teaching hospitals was made, with similar findings. Contraception in women over 49 years of age is unnecessary.

This study investigated the frequency and fate of pregnancy after the 45th birthday, with determination of the incidence of induced and spontaneous abortion and an analysis of maternal complications, fetal abnormalities, and the occurrence of hydatidiform mole.

At Columbia Hospital for Women from June 1967 to December 1972 there were 28,796 deliveries with nine patients who were 45-48 (a rate of three per 10,000). There was one pri-

This study investigated the frequency and fate of pregnancy after the 45th birthday with determination of induced and spontaneous abortion and an analysis of maternal complications, fetal abnormalities, and the occurrence of hydatidiform mole.

migravida, delivered by Cesarean Section which was followed by postpartum psychosis. All others were delivered vaginally with no complications. All babies, including one set of twins, had excellent APGAR scoring. Imperforate anus was diagnosed in an infant with immediate surgical care and complete recovery. The follow-up study revealed six of nine babies were living and well. The other three were lost to follow-up.

There were 11,057 abortions with 40 in patients over the age of 45; 18 were induced and 22 were spontaneous, including five hydatidiform moles. The total number of induced abortions during this period was 7,397, with 18 patients 45 to 51 years of age: an incidence of 0.25%. This compares with the JPSA* report of 42,598 patients with an incidence of 0.2%.

An analysis of pregnancies in the over 45 age group was made for three

years 1970-1972 comparing Columbia Hospital with a group of five large teaching Hospitals (CPHA**). There were 14,420 total deliveries at Columbia Hospital with six women 45 years or older as compared to the combined 5 Hospitals with 28,200 deliveries and 14 patients 45 years or older. The ratio per 10,000 was approximately the same, as were the ratio of Cesarean Sections.

There were no maternal deaths, no retained placentas, postpartum hemorrhages, umbilical cord prolapse or amniotic fluid embolisms. There were three cases of antepartum hemorrhage and only one instance of prolonged labor.

There were 5,710 induced abortions at Columbia Hospital with 14 patients

* C. Tietze and S. Lewis—Joint Program for the Study of Abortion (Interim Report).

** A large Hospital is defined as having 15,000 or more discharges per year by CPHA. Basic data for use in this study were supplied by Commission on Professional and Hospital Activities (CPHA), Ann Arbor, Michigan. In these data the identities of individual hospitals were not revealed in any way. Any analysis, interpretation, or conclusion based on these data is solely that of Columbia Hospital for Women, and CPHA specifically disclaims responsibility for any such analysis, interpretation or conclusion.

PREGNANCY AFTER AGE 45

KUSHNER

45 years or older, a ratio of 2.5 per thousand. The combined Hospitals had 2,324 induced abortions with five patients in the same age group for a ratio of 2.1 per thousand. There were no deaths in either group.

There were 1,565 patients with spontaneous abortion; eight of whom were 45 years or older at Columbia Hospital with a ratio of 5.1 per thousand. The combined Hospitals had 3,308 patients in the same category with 15 patients in the over 45 age group for a ratio of 4.6 per thousand.

There were two hydatidiform moles in the Columbia Hospital group (16.7%) and one in the CPHA group (5.3%).

Discussion

At Columbia Hospital in the six year period from 1967-1972 there was a total of 38,693 women admitted with a diagnosis of pregnancy. Only 49 were beyond their 45th birthday. The oldest woman having a viable birth was 48 years old. There was one patient 51 years of age with a hydatidiform mole.

The probability of pregnancy occurring in women past their 45th birthday should be discussed in detail by the gynecologist. The decreasing necessity of contraception after age 45 should be evaluated with the possible complications occurring with the use of the birth control pill and IUD. After a thorough discussion, the patient should be allowed to exercise her option. After age 48, the possibilities of pregnancy are extremely slight, and are practically non-existent after age 49.

Many women will continue to menstruate in their sixth decade and may even ovulate, but do not become pregnant due to an inadequate corpus luteum.¹ Novak also states that after the age of 50, the woman is more apt to be struck by lightning than become pregnant. There is no doubt that

women can deliver normal infants after age 45, but the stress and strain of infant care should be a discouraging factor except in unusual circumstances.

Emotional disturbance in women approaching the menopause beyond 48 years can frequently be best treated by reassurance of her sexuality and an open discussion of her fear of pregnancy. Discontinuance of the use of diaphragms and condoms for contraception in this group of patients will frequently be followed by a renewed interest in sexual relations.

Summary

There were 28,796 deliveries with nine patients in the 45-48 year age group. There were 11,057 abortions of which 40 were in patients over the age of 45. There were very few complications in the over 45 age group during parturition. The difficulty of caring for babies at home may present a problem, particularly in the primigravida. Pregnancy with viable births after age 48 occur so infrequently in the U.S. that the reliability of a recorded older age must be questioned.

References

1. NOVAK, E. R.: Ovulation after Fifty. *Obstet. Gynecol.*, 1970, 36:903-910.

Dr. Kushner, Senior Consultant, Columbia Hospital for Women and Clinical Professor, Obstetrics and Gynecology, Georgetown University Hospital, Washington, D.C.

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Premature Menopause: A Report of Two Cases

RICHARD J. FALK, M.D.

Abstract

Premature ovarian failure was diagnosed in two young women seen at Columbia Hospital for Women in the last six months. Possible etiologies of the condition are discussed; many of these can now be identified due to the availability of new and specific diagnostic techniques.

Introduction

The patient with secondary amenorrhea presents a clinical challenge encountered frequently by every gynecologist. The investigation of such patients should define the defect in cessation of menstruation, and determine if and how this defect can be modified. This gains new importance in light of recent advances in reproductive medicine, rendering treatable conditions which were previously refractory to therapy. Careful administration of exogenous gonadotropins can result in ovulation with subsequent pregnancy in patients with hypogonadotrophic hypogonadism. Loss of the rhythmicity of the hypothalamic-pituitary-ovarian axis, such as occurs in "sclerocystic ovarian syndrome" or "post-pill amenorrhea," can be corrected by the proper use of clomiphene citrate.

There are, however, situations which are not amenable to successful induction of ovulation. Premature

There are situations which are not amenable to successful induction of ovulation. Premature ovarian failure, or premature menopause, is such a condition, now more easily recognized with the aid of the present availability of accurate hormone determinations, endoscopy and cytogenetic studies.

ovarian failure, or premature menopause, is such a condition, now more easily recognized with the aid of the present availability of accurate hormone determinations, endoscopy and cytogenetic studies. It is the purpose of this paper to present two such cases seen in the past six month period.

Case Reports

Case 1. J. R., a 20 year old woman who was gravida 1, ab 1, was referred to Columbia Hospital for Women for evaluation of secondary amenorrhea. Shortly after her menarche, at age 13, she became pregnant. This was terminated by a criminal abortion with subsequent septic endometritis. Uterine curettage and antibiotic therapy produced an uneventful recovery. She was placed on oral contraceptives which she continued to take, with monthly withdrawal bleeds, until age 17. Following discontinuation of the

drug, she remained amenorrheic to the present time. Her past medical history included removal of a thyroid adenoma at age 16. She was on no medications. Her family history gave no previous instances of premature menopause; all family members were tall and thin.

On physical examination she was a tall (70 3/4"), thin (114 1/2 lbs.) black woman. Her blood pressure was 130/75, her pulse 72 and regular. The skin was normal and there was no excessive hirsutism. Her eyes were normal (fundus, lenses). The neck showed a transverse scar; the thyroid was normal to palpation. The lungs were clear, the heart showed a grade I/VI systolic murmur along the left sternal border, without cardiomegaly. The abdomen showed no organomegaly. On pelvic examination there was a small urethral caruncle, the vagina mucosa was pale, with flattened rugae. There were no cervical lesions, the uterus was of normal size and freely mobile. The adnexa were not palpable. The cervical mucus was scant, with no spinnbarkeit or ferning, the vaginal smear showed atrophic cells.

In the laboratory, the serum follicle stimulating hormone level was 134 milli international units per ml, the serum luteinizing hormone 55 milli international units per ml. Cortisol at 8:00 a.m. was 10.4 ug per 100 ml.; at 4:00 p.m. 6.2 ug per 100 ml. The T-4 was 6.5 ug per 100 ml. Chromosomal analysis (peripheral blood) showed 46

PREMATURE MENOPAUSE

FALK

XX. A sella turcica X-ray was normal. Review of the slides from the curettage in 1968 showed necrotic products of conception and endometritis.

The patient underwent diagnostic laparoscopy. A normal sized uterus and small, atrophic, white ovaries with typical postmenopausal rugated surfaces were observed. Biopsies from neither ovary showed follicles or ova (Figure 1). A single corpus albicans was present.

The patient is being maintained on cyclical estrogen with progestational withdrawal.

Case 2. J. C. is a 33 year old nulligravida who was seen at Columbia Hospital for Women for evaluation of amenorrhea of 13 years' duration. Her menarche was at age 13, with normal menses until 1961 (age 20) when she became amenorrheic. She was evaluated elsewhere, where her amenorrhea was at first felt to be secondary to emotional trauma. Ovarian failure was diagnosed when her urinary gonadotropins were found to be elevated (100 R.U.) with no detectable urinary estrogens. She was cycled on estrogen and progestin with regular withdrawal bleeding. Subsequently, several attempts at ovulation induction were made utilizing corticosteroids and clomiphene citrate. When these failed, she was referred to Columbia Hospital for Women for evaluation and possible treatment. Her past medical history was not contributory, and there was no family history of premature menopause.

On physical examination she was 62 3/4" tall and weighed 120 pounds. Her blood pressure was 120/70. Her hair and skin were normal, her head, ears, nose and throat were normal. Her lungs were clear, her heart normal. The breasts were normal, her abdomen showed no organomegaly. On pelvic examination the introitus was normal, the vaginal mucosa was pale pink with flattened rugae; the cervix was small,

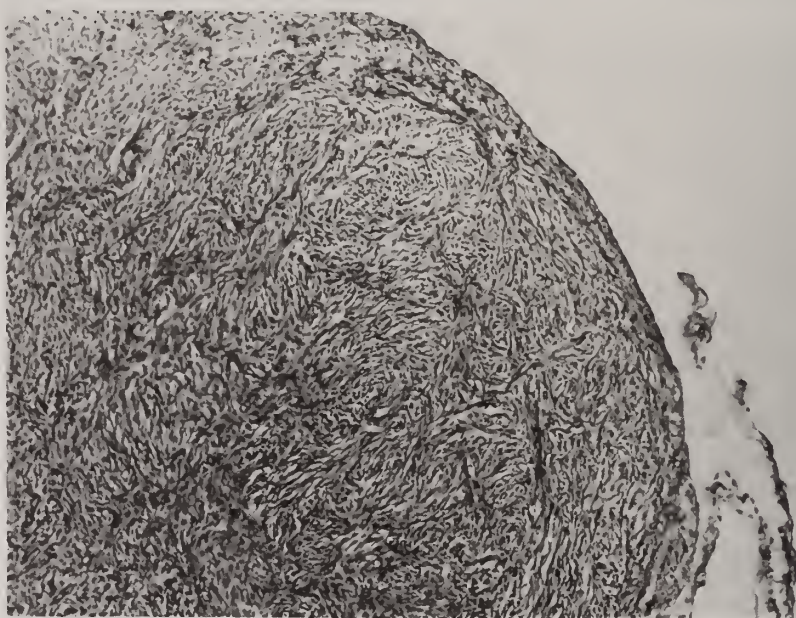


Fig. 1. Biopsy of ovary showing lack of follicles.

with scant nonferning cervical mucus. The uterus was of normal size, and the adnexa were normal.

In the laboratory, re-evaluation revealed a menopausal level of serum luteinizing hormone (86 milli international units per ml.).

Discussion

Ovarian failure occurring spontaneously between ages 45 and 55 is called menopause. When menopause occurs prior to age 40, it is considered premature, and such deviations from normal have aroused much curiosity. Sporadic reports have been made on this condition since the early part of this century, many presenting various conditions resulting in ovarian failure, and frequently not separating these entities from apparently spontaneous cessation of ovarian function.

Keettel and Bradbury¹, in their series of 24 young women with premature ovarian failure, stated that the

incidence of this condition approached that of the polycystic ovarian syndrome. Their study, however, lacked both cytogenetic evaluation and, in most cases, histologic studies on the ovary, and may well have included women with congenitally abnormal gonads.

It is known² that women with various forms of gonadal dysgenesis may have ovulatory menstrual periods for several years, and may even achieve pregnancy. Inclusion of this group with those who apparently have morphologically normal but senile gonads will give a falsely elevated incidence for premature menopause.

Kinch *et al*³, using open ovarian biopsy, endocrine evaluation and chromosomal karyotype, found seven patients with normal chromosomes whose ovaries lacked follicles in a study of 24 women with primary gonadal failure. The remainder of the patients had either chromosome anomalies or morphological defects in the

gonads. *i.e.*, hypoplasia or dysplasia.

Emperaire *et al*⁴ reported on seven women between the ages of 14 and 25 with secondary amenorrhea due to ovarian failure. The karyotype was normal in five of the seven patients, three had "ovarian streaks", and in two the ovaries were the typical small, wrinkled postmenopausal gonads.

Familial occurrence is recognized as an etiologic factor in this condition; however, neither of the patients discussed had any such familial disposition.

It is intriguing to note that in Case 2 emotional stress may have precipitated her amenorrhea. Emperaire *et al* also had such a case, and speculate about nervous control of ovarian function, bypassing the hypothalamus.

The present accessibility of radioimmunoassays of peptide and steroid hormones can usually localize the hormonal defect in an amenorrheic patient, and identify those with ovarian failure. Determinations of the karyotype in this group will isolate those with chromosomal abnormalities, and identify patients who would benefit from gonadectomy (those with

a Y chromosome). Finally, diagnostic laparoscopy with ovarian biopsy decreases the risks of "unjustified laparotomy"¹ and "open" ovarian biopsy, yet satisfies Emperaire's criteria for the diagnosis of ovarian failure (which include histologic evaluation).

The diagnosis of irreversible ovarian failure, now clinically practical, is of utmost importance to avoid time consuming, expensive and entirely futile attempts at ovulation induction.

References

1. KEETTEL, W. C., BRADBURY, J. T.: Premature Ovarian Failure; Permanent and Temporary, *Am. J. Obst. & Gynec.* 1964, 89:83.
2. BAHNER, G., SCHWARTZ, G., HARN-DEN, D. G., JACOBS, P. A., HIENZ, H. A., WALTER, K.: A Fertile Female with XO Sex Chromosome Constitution, *Lancet* 1960, 2:100.
3. KINCH, R. A. H., PLUNKETT, E. R., SMOUT, M. S., CARR, D. H.: Primary Ovarian Failure, *Am. J. Obst. & Gynec.* 1965, 91:630.
4. EMPERAIRE, J. C., AUDEBERT, A., GREENBLATT, R. B.: Premature Ovarian Failure, *Am. J. Obst. & Gynec.* 1970, 108:445.

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THE VIEW BOX

Prepared by
The Department of Radiology
Washington Hospital Center

A 44 year old white female was evaluated for intermittent abdominal pain and episodic bouts of diarrhea. She denied anorexia, weight loss or bleeding.

(for diagnosis see page 529)



Mixed Mesodermal Tumors of the Corpus Uteri

WILLIAM J. JAFFURS, M.D., DOUGLAS G. MARTZ, M.D., STEELE STEWART, M.D. AND J. KEITH CROMER, M.D.

Abstract

Mixed mesodermal tumors of the uterus are uncommon. It is one of the most aggressive malignancies of the female genital tract. Twenty patients have been diagnosed with this unusual neoplasm at Columbia Hospital for Women from 1963 to 1974, while at the same time, 1,227 malignancies of all types arising in the female genital tract have been primarily diagnosed and treated at the same institution. It is of interest to review the case histories—and to determine the results of therapy.

In our series of 20 patients with mixed mesodermal tumors of the uterus seen at Columbia Hospital for Women between 1963 and 1974, the youngest woman with this disease was 47 years old, the oldest 84. Four of the women were black and sixteen were white. Gravidarity was unremarkable. Seven patients gave a positive family history for some type of malignancy, eight gave a negative response and in five it was not determined. Four had received estrogens for menopausal symptoms. Only one patient had a previous malignancy, and that was of the breast; she had received radiation therapy to the chest wall and axilla. None of the other nineteen had ever been exposed to x-rays except for diagnostic purposes.

Eighteen patients had unexplained post menopausal vaginal bleeding and two had necrotic masses protruding from the uterus or vagina. Fifteen of the patients had the diagnosis estab-

Histologic studies show that the malignancy is composed of two primary cellular elements, epithelial and mesenchymal or stromal components. These two components will both show a range of malignant changes that may be independent of each other's degree of cellular differentiation.

lished on tissue recovered by dilatation and curettage. One patient had a failure of dilatation and curettage and the diagnosis was made following hysterectomy with consultation by the pathologist prior to closure of the abdominal wall. Two patients had the malignancy diagnosed following hysterectomy for enlarged pelvic tumors with uterine bleeding. The two patients who presented protruding vaginal or uterine masses underwent biopsy and frozen section examination for diagnosis.

Histologic examination showed that the neoplasms were composed of varying amounts of two malignant tissue elements, adenocarcinoma and sarcoma. The adenocarcinoma element varied from a well differentiated or papillary type to a poorly differentiated, barely recognizable adenocarcinoma. Sarcoma tissue elements were observed growing either between the malignant epithelial components or growing as polypoid protruberances admixed with sparse epithelial ele-

ments. In a few areas, it was difficult to distinguish carcinoma from sarcoma. When the sarcoma was clearly identifiable, it could be divided into two types (either homologous or heterologous). When the latter condition was present chondromatous or rhabdomyomatous cellular elements were observed. When metastases were examined they contained predominantly sarcoma with recognizable epithelial malignant components. When the uteri were removed and examined, they were enlarged and contained characteristic polypoid masses, some of which protruded into the endometrial canal or into the endocervical cavity and beyond to dilate the cervix. In one instance the tumor protruded into and distended the vaginal cavity. The polypoid tumor nodules were usually globular, slightly irregular, and hemorrhagic with extensive necrosis. Only a few of the tumors were confined to the uterine cavity. The majority showed either superficial or deep myometrial invasion. Six showed evidence of metastases at the time of primary tissue diagnosis.

The patients were treated by either surgery, radiation, chemotherapy, or some combination of these methods. Five patients were treated with total abdominal hysterectomy with bilateral salpingo-oophorectomy. Three are alive without evidence of disease, one is dead of the disease, and the other is lost but was free of the disease at last contact. Two patients were treated with radiation alone; both are dead due to their malignancy. Eight patients

MIXED MESODERMAL TUMORS OF THE UTERUS

JAFFURS, MARTZ, STEWART AND CROMER

were treated with surgery and chemotherapy; six are dead of the neoplasm. Two were free of the disease at the last contact. One was treated with radiation and chemotherapy and died of the disease. One patient was treated with surgery, radiation, and chemotherapy and is dead of the disease. Three patients were treated with surgery and radiation: two are dead of malignancy and one is alive with no evidence of disease.

With respect to the quality and length of survival, one patient died within a month of primary diagnosis, nine patients died within 12 months and three succumbed within two years. Of the seven living patients, five are alive and clinically free of malignancy, one is alive with metastatic disease, and one is lost to the study group.

Discussion

Sarcomas as a group are reported to occur as 1-2% of all malignant uterine tumors¹. Mixed mesodermal tumors of the uterus are rare malignant tumors that arise from multi-potential endometrial stromal cells found in the genital ridge about the Mullerian duct. These cells can form both mesenchymal and glandular components. There is no clear agreement on the proper classification of these malignancies^{1 & 2}. Some prefer the term mixed mullerian tumor to mixed mesodermal tumor, because of the presence of either homologous endometrial stromal elements or the heterologous stromal elements such as striated muscle, cartilage, osteoid, adipose, or myxomatous tissue. This point is important as it is used as one of the indicators of prognosis, which is usually worse if heterologous cellular elements are recognized in the neoplasm.

The gross pathologic changes are characteristic. The uterus is generally enlarged by polypoid yellowish soft or

necrotic tumor masses. These may be single or multiple and fill or distend the uterine cavity. They may protrude into the endocervical canal and dilate the cervical os, and ultimately project into the vagina. Superficial or deep myometrial invasion must be searched for.

Histologic studies show that the malignancy is composed of two primary cellular elements, epithelial and mesenchymal or stromal components. These two components will both show a range of malignant changes that may be independent of each other's degree of cellular differentiation. Care must be taken to determine what mesenchymal elements are present. If the sarcoma is pure and not a type "foreign" to the uterus that is considered the homologous type. If the sarcoma elements are heterologous, examination must establish their identity. These mixtures may be of rhabdomyosarcoma, chondrosarcoma, liposarcoma or osteosarcoma.

The patient whose tumor has spread beyond the limits of the uterus or has deeply invaded the uterine wall has a poor prognosis. A number of authors have concluded that the extent of the malignancy at the initial diagnosis is probably the most significant factor affecting the survival of the patient^{3,4,5, & 6}. Williamson and Christopherson reported a survival rate of 20.5% for five years.⁷ In our treated group of 20 patients 13 died within two years. Six are still alive; one has metastatic disease, whereas the other five are currently free of disease. In these cases, the neoplasm was either limited to involvement of the uterine cavity or only invaded the superficial aspect of the myometrium. One patient was lost to the study. She had superficial invasion of the uterus, and was alive and asymptomatic at the last examination.

There is no consistently reliable method of treatment. Hormonal therapy is of no help. Chemotherapy alone

is of little aid. Radiation has been advocated pre-operatively or post operatively, but does not uniformly affect survival^{8 & 9}. Total abdominal hysterectomy and bilateral salpingo-oophorectomy remains the method of choice.

References

1. KEMPSON, R. L.: Sarcomas and related neoplasms, *The Uterus*, 1973, Chapt. 15:298-319.
2. BAGGISH, M. S.: Mesenchymal tumor of the uterus. *Clin. O.B.-Gyn.*, June, 1974, 17, 51-88.
3. BARTSICH, E. G., O'LEARY, J. A., MOORE, G. J.: Carcinosarcoma of the uterus. *Obstet. Gyn.*, 1967, 30, 518.
4. CHUANG, J. T., VANVELDEN, J. J., GRAHAM, J. B.: Carcinosarcoma and mixed mesodermal tumors of the uterine corpus. *Obstet. Gyn.*, 1970, 35, 769.
5. NORRIS, H. J., ROTH, E., TAYLOR, H. B.: Mesenchymal tumors of the uterus. II. A clinical and pathologic study of 31 mixed mesodermal tumors. *Obstet. Gyn.*, 1966, 28, 57-63.
6. NORRIS, H. J., TAYLOR, H. B.: Mesenchymal tumors of the uterus., III. A clinical and pathologic study of 31 carcinosarcomas. *Cancer*, 1966, 19, 1759-1765.
7. WILLIAMSON, E. O., CHRISTOPHERSON, W. M.: Malignant mixed mullerian tumors of the uterus. *Obstet. Gyn. Surv.*, 1972, 27, 743.
8. RACHMANINOFF, N., CLIMIE, A.R.W.: Mixed mesodermal tumors of the uterus. *Cancer*, 1966, 19, 1705.
9. OBER, W. B., TOVELL, H. M.: Mesenchymal sarcomas of the uterus. *Am. J. Obstet. Gynec.*, 1959, 77, 246.

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Leiomyomata with Aplasia of the Uterus and Fallopian Tubes: A Case Report

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Abstract

A rare case of leiomyomata with aplasia of the uterus and Fallopian tubes is presented together with a brief description of the genital anomaly and a discussion of the possible origins of the tumors.

Agenesis of the uterus is a condition not infrequently reported in the medical literature, usually in association with urinary tract anomalies¹ and with total or partial agenesis of the vagina. The presence of leiomyomata in the absence of the uterus engenders considerable interest, raising questions as to the histogenesis of these tumors.

Congenital absence of the uterus with development of the vagina and adnexae,² albeit rudimentary, presupposes failure of fusion of the intermediate portions of both Mullerian ducts with development of the upper and lower portions. The Fallopian tubes arise from the cranial portion,³ the vagina from the caudal portion of the ducts. Since the ovaries are unrelated to the above structures and arise from the sex gland anlage⁴ on the anterior surface of the mesonephron, they are not involved in the developmental defect.

Case Report:

Mrs. A. A., a 49-year-old black female with known pelvic tumors,

Aplasia of the uterus and the Fallopian tubes with preservation of the vagina represent a complete failure of development of the intermediate and superior portions of the Mullerian ducts. Such an anomaly occurring in association with leiomyomata raises questions as to the origin of these tumors.

came for examination on 8/18/71. She had never menstruated and had had no vaginal discharge. In 1949, she had undergone surgery to determine the cause of her amenorrhea. She was told she had an "infantile paralysis" of the womb. In 1958, a thyroidectomy and surgery for benign breast masses were performed. In 1968 she was told that she had pelvic tumors and would require surgery.

Physical examination revealed a well developed, well nourished, and alert black female. The breasts were well developed. The distribution of pubic and axillary hair seemed normal. There was some tenderness on palpation over both right and left quadrants of the abdomen.

The clitoris, urethra, labia majora and minora were within normal limits. The vaginal introitus was marital, and the vagina was adequate but ended in a

pouch and had normal appearing mucosa. Bimanual examination disclosed a firm pelvic mass on the right side which was approximately three inches in its greatest diameter. A similar smaller mass approximately two and one-half inches in diameter was present on the left side. The uterus could not be felt nor could the cervix be seen. A diagnosis of congenital absence of the uterus and bilateral pelvic masses was made.

An exploratory laparotomy was performed. The uterus was absent. There was a small fibrous mass covered with peritoneum situated behind the bladder. This fibrous structure, approximately 2.5 cm. in width, was continued laterally on each side of the pelvis to terminate in what appeared to be fibroid tumors. On the right side a nodular mass 9 x 7 cm. was found to be arising from a rudimentary uterine horn. Similarly, a smaller nodular mass approximately 3 x 2.5 cm. was noted in a vestigial structure on the left. The ovaries were small, 3 x 1 cm., and appeared normal. There was no evidence of recent ovulation.

Both ovaries, fibroids and the vestigial tissues and mid-line fibrous structure were surgically resected.

On pathologic examination, the mid-line structure (measuring 2.5 cm. in length by 1.7 cm. in width and 0.9 cm. in thickness) was felt to be a hypoplastic or aplastic uterus. There

LEIOMYOMATA WITH APLASIA OF UTERUS AND TUBES

CROMER, JAFFURS AND MARTZ

was no recognizable cervix nor endometrial cavity. The vestigial structure, which resembled a right Fallopian tube, measured $3 \times 1.5 \times 1$ cm. It gave rise at its medial end to a fibroid measuring $9 \times 7 \times 6.5$ cm, and weighing 160 grams. This had a typical histologic appearance for leiomyoma. The right ovary measured 5 cm. in length and up to 1.3 cm. in width and 0.7 cm in thickness. It appeared inactive. Attached to the ovary were structures which were considered to be fimbria. On the left side, there appeared to be at least three separate fibroids with a probable rudimentary Fallopian tube stretched over one aspect of the fibroid with the other end extending into a mass of fimbria-like structures. The left ovary was smaller and measured $2.4 \times 1.4 \times 0.9$ cm. There were no grossly obvious follicular structures or recent corpora within the tissue. Figure 1 illustrates the gross specimen.

The mid-line structure suspected of being hypoplastic uterus contained a single gland space resembling an endometrial gland, but was without definite stromal elements. This is illustrated in Figure 2. No cervical elements were discovered. Studies of the rudimentary Fallopian tubes showed only occasional structures which resembled mesonephric duct remnants. The ovaries contained numerous old corpora albicantia (Figure 3)

Discussion:

Congenital aplasia of the uterus which results from non-union of the intermediate portions of the Mullerian ducts is a recognized anomaly.³ The uterus as such is absent. The Fallopian tubes are present in the pelvis and terminate blindly near the mid-line behind the bladder. The mesial ends of the tubes often form bulbous enlargements representing rudimentary uterine horns. The vagina may be normal,



Fig. 1. Agenesis of the uterus with leiomyomata arising from rudimentary adnexae.

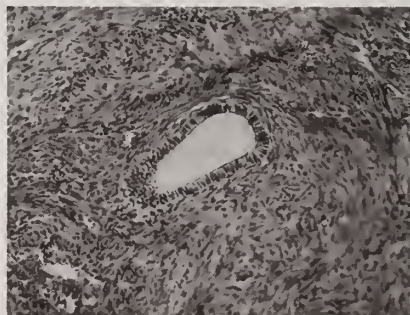


Fig. 2. One gland space from midline mass which resembles an endometrial gland, although stromal elements are lacking.

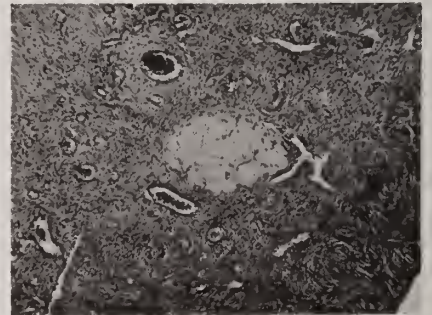


Fig. 3. Post-menopausal ovary with corpora albicantia.

or the upper third may be missing. Congenital absence of the uterus is most frequently associated with anomalies of the urinary tract.

Aplasia of the uterus and the Fallopian tubes with preservation of the vagina, as in this case, represent a complete failure of development of the intermediate and superior portions of the Mullerian ducts. Such an anomaly occurring in association with leiomyomata raises questions as to the origin of these tumors. Uterine fibroids with agenesis of the uterus have been reported. In the one case described by Wharton¹ the leiomyomata developed from rudimentary uterine horns, which were clearly identifiable. In one of the rudimentary horns there was a tiny menstruating uterus. Similar findings were not present in this case. There were no identifiable uterine horns or well defined identifiable Fallopian tubes in the surgical specimen. All that can be said about the origin of the tumors in this case is that they originated in the soft tissue of the vestigial adnexae. One might speculate that rudimentary uterine anlagen were present and had been completely replaced by leiomyomata. Further speculation suggests that the tumors arose from Wolffian or mesonephric duct derivatives which were present in the specimen. This speculation seems far-fetched since such findings have never been recorded in the literature. The idea that the tumors might have arisen from blood vessels present in the soft tissue of the adnexae is not to be discarded. Indeed, one theory^{5,6} holds that uterine fibroids arise from immature muscle cells (genitoblasts) usually lying dormant in muscle bundles in the vicinity of uterine blood vessels. Under appropriate stimulation via estrogen these cells product fibroids. While this theory is not completely accepted, it might be applicable to the origin of the tumors in this case. In any event, the tumors, regardless of their origin,

arose from vestigial adnexae with aplasia of the uterus. This is a rare complication of a genital anomaly.

References:

1. WHARTON, L. R.: Embryological and Congenital Malformations, Gynecology including Female Urology, 2nd Edition, 1947, Pub. W. B. Saunders, Phila., Pa.
2. GORGAN, R. L., BLOCKER, T. C.: Agenesis of Mullerian ducts with Report of a Case, Amer. Jr. Ob & Gyn, 1946, 72:212.
3. FOLLIGSTAD, A. H.: Polycystic Ovaries with Absence of Uterus in a Child, Rocky Mt. Med. Jr., 1956, 53:465.
4. WEI, EUNG-PIN: Congenital Absence of Uterus, Jr. Formosan Med. Assn., 1966, 65:51.
5. MILLER, N. F., LUDOVICI, P.: On the Origin and Development of Uterine Fibroids, Amer. Jr. Ob & Gyn, 1955, Vol. 70, No. 4, P. 720.

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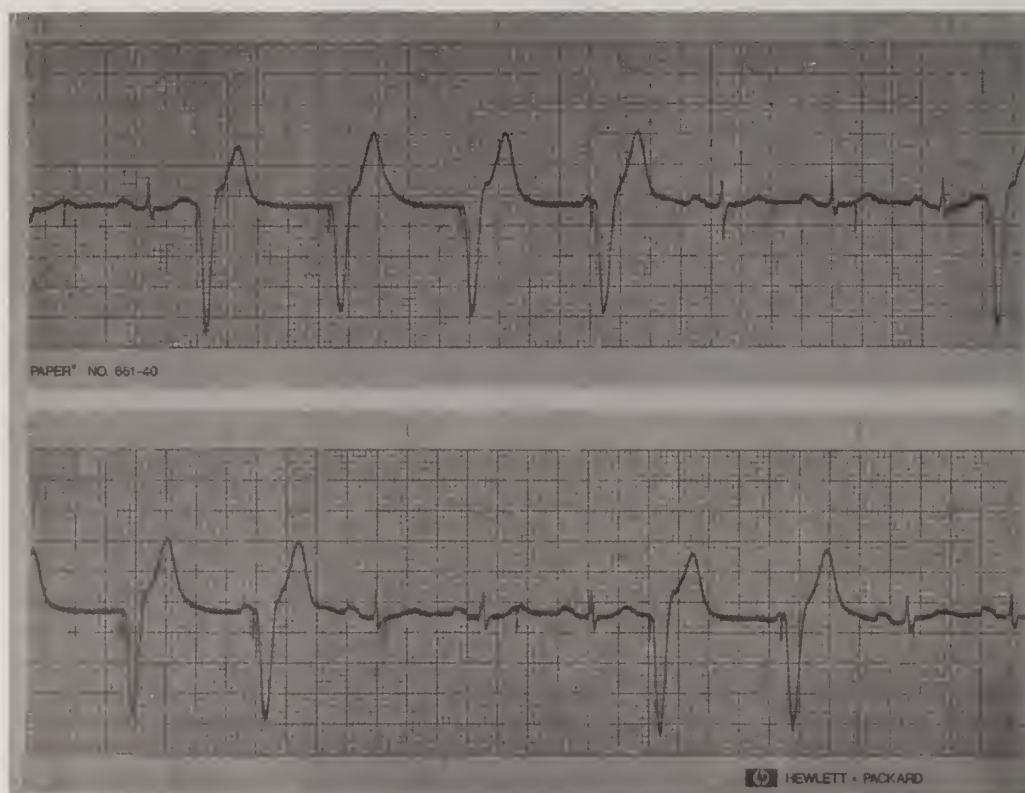
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ECG PROBLEMS

HISTORY: A 72-year-old white female is seen as an outpatient for evaluation of the function of a pacemaker. This electrocardiogram was taken with a magnet held over the pulse generator.

(for diagnosis see page 529)



Colposcopic Evaluation of Stilbestrol Exposed Young Women

JOHN L. MARLOW, M.D.

Abstract

The historical background relating to the use of stilbestrol during pregnancy for the treatment and prevention of complications of pregnancy is reviewed. Evaluation and followup of exposed young women is discussed with special emphasis upon the value and use of colposcopy. Although cancers which may occur in the genital tract in these young women are rare, they may behave in a virulent fashion. The frequency of asymptomatic cases, as well as the unreliability of vaginal cytology for detection, support the value of screening young women after menarche if they have been exposed prenatally to stilbestrol or similar drugs.

Introduction

The recent association between maternal ingestion of diethylstilbestrol during pregnancy and the subsequent development of vaginal and cervical malignancies in young girls born to these women poses the problem of evaluation and followup of these patients. The exact number of women treated with diethylstilbestrol (DES) and similar nonsteroidal synthetic estrogens during pregnancy is not known. Dr. Heinonen⁶, of the Boston Collaborative Drug Surveillance Pro-

The recent association between maternal ingestion of diethylstilbestrol, during pregnancy, and the subsequent development of vaginal and cervical malignancies in young girls born to these women poses the problem of evaluation and followup of these patients.

gram, estimates that an average of 100,000 DES prescriptions were written each year from 1960-1970 when statistics were available and some 20 years after the peak usage of the drug. Estimates of the total reported population of young women exposed is between 500,000 and one million. The total number of reported malignancies of this at risk population is small, now less than 200.^{1,11}

Dr. Herbst and co-workers⁴ in 1972 observed:

1. The period of greatest risk may be soon after abnormal vaginal or cervical epithelium has been stimulated at the onset of puberty.
2. Many patients are asymptomatic, and although vaginal bleeding, staining, or discharge led to discovery of most of the tumors, cytology alone was not a reliable means of diagnosis.

3. Screening examinations of the population at risk are indicated.

The purpose of this paper is to review the history of this new disease syndrome and emphasize the values and importance of colposcopy in its diagnosis and followup.

History

Diethylstilbestrol was first introduced to clinical medicine in 1938 by Dodds *et al*¹⁰. Its popularity related to the fact that it was very potent, highly active by mouth, and had a long duration compared with the available estrogen compounds. By virtue of its synthetic derivation, it was both cheap and plentiful. In 1948, Dr. O. Watkins Smith¹ of the Free Hospital for Women in Boston reported 632 pregnancies delivered by 117 obstetricians who prescribed DES for the treatment and prevention of complications of pregnancy. Patients with threatened abortion, a history of previous abortion, or diabetes mellitus were included in the study. The suggested treatment regime was 5 mg. orally daily beginning 6-7 weeks from the last menstrual period. This was increased at 5 mg. increments every two weeks up to 15 weeks gestation. At that time, the dose was increased by 5 mg. a week and discontinued at 35 weeks, the final dose usually being 125

COLPOSCOPIC EVALUATION OF STILBESTROL EXPOSED WOMEN

MARLOW

mg. per day. In some cases up to 200 mg. daily was given. By comparison, the usual castration replacement dosage of DES is 0.2 to 0.5 mg. daily.

This report stimulated widespread use of DES for the treatment and prevention of complications of pregnancy. At the Boston Lying In Hospital, for example, between 1946 and 1951, 675 of 14,500 deliveries or one in 21 patients received DES treatment during their pregnancy. Twenty years later the first published reports were made suggesting an association between DES and genital tract neoplasms in young women whose mothers received this drug during their pregnancy.

Drs. Herbst and Scully² in 1970 described a relationship between maternal stilbestrol therapy and tumor appearance of adenocarcinoma of the vagina. In their retrospective study, eight patients with adenocarcinoma of the vagina born in New England hospitals between 1945-51 were described. In these hospitals, this malignancy had not been previously reported in this age group. Maternal bleeding and previous pregnancy loss were noted to be more common in the study group. Data was compiled concerning multiple factors in the pregnancies and included maternal age, smoking, bleeding during pregnancy, prior pregnancy losses, estrogen treatment, breast feeding, X-ray exposure, birth weight, menarche, complications and outcome of pregnancy, ingestion of other medications during pregnancy, childhood diseases (maternal and patient), household pets, cosmetics, alcohol ingestion, occupation, and years of education of parents. A significant relationship was established between maternal estrogen therapy during pregnancy, a history of bleeding, and prior pregnancy loss.

Subsequent to their initial report, a Registry of Clear-Cell Adenocarcinoma of the Genital Tract in Young Females

was established and cases of this malignancy occurring in women under the age of 30 are being accumulated. A review of these cases was presented to The American College of Obstetricians and Gynecologists in 1973.⁵ The age span reported was 8-25. Stilbestrol, dienesterol and hexestrol, all non-steroidal synthetic estrogens, have been implicated. As little as 1.5 mg. of DES daily taken throughout pregnancy and ingestion for as little as 10 days during the first trimester have both been associated with tumor appearance in the offspring. Since the establishment of the Registry, the total number of cases of carcinoma reported remains small (less than 200) and in view of the large number of women who were treated during pregnancy, the risk of development in any exposed female at the present time appears small.

Symptoms

According to Drs. Stafl and Mattingly,⁹ 87% of patients with anatomical alterations of the genital tract associated with DES may be asymptomatic, 10% may have a mucous discharge and another 3% may note a burning or a discomfort after coitus. Irregular bleeding or unusual cases of staining from the vagina prior to the menarch should alert the physician to the need for examination of the genital tract.

Examination

It is our policy that all postmenarchal females whose mothers took DES or similar compounds during pregnancy have a complete pelvic examination, including colposcopy and cytology. If the child is younger when the gynecologist first becomes aware of the maternal history, some contact between the physician and the patient or her family should be maintained

and the patient should be thoroughly examined if any abnormal symptoms develop. In the very young patients with intact hymen, a laparoscope may be used to inspect the vagina and cervix. Cytology cannot be relied upon alone; up to 30% malignancies may have negative cytologic examinations.

Colposcopy

Colposcopy provides a stereoscopic magnified view of both cervix and vagina. Blood vessel patterns are noted under green light and a typical epithelium may be seen. A solution of 3-4% acetic acid is then applied. This causes the architecture of the epithelium to become more visible. An iodine stain is then applied using Schiller's solution. Directed biopsies may be taken to determine the presence of adenosis or any nuclear atypicality. Lesions with nuclear atypicality, even without being frankly malignant may be surgically excised. Gross anatomical changes of the cervix may be seen including those described as erythroplakia and cervical eversion, and as vaginal "collars", "hoods", and "cock's comb". (Fig 1-4)

Adenosis

Adenosis, the finding of tall mucin producing cells in the vaginal wall was first reported by von Preuschen⁷ in 1877. As late as 1940, one of the largest series in the literature was of three cases, by Plant and Dreyfuss⁸. The youngest patient was 25 years of age. The incident of adenosis in the stilbestrol exposed young women has been reported from 30% to 91%.⁹ The higher figure relates to the more effective detection available through the use of the colposcope. Adenosis has been noted in proximity to clear-cell adenocarcinoma; however, clear-cut histologic transformation from adenosis to adenocarcinoma has

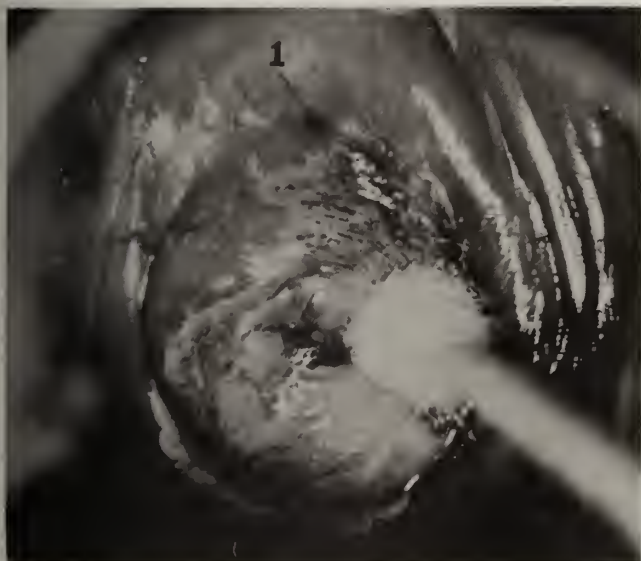


Fig. 1. Cervix and Vaginal Fornix Adenosis (1).



Fig. 2. Vaginal Wall. Iodine (Shiller's) non-staining squamous epithelium (1). Adenosis gland opening (2).



Fig. 3. Cervix. External OS (1) portio vaginalis of cervix. Collar or hood (2).



Fig. 4. Cervix. Columnar epithelium with squamous metaplasia (1).

COLPOSCOPIC EVALUATION OF STILBESTROL EXPOSED WOMEN

MARLOW

not been demonstrated. The correct management of patients with adenosis in the absence of atypia has not yet been established. Our current approach in the absence of symptoms or atypia is close observation and periodic colposcopic examination. Intra-vaginal application of estrogen, progesterone, acid promoting solutions or jels, surgical extirpation and cautery have been recommended but the value of these treatments remains to be demonstrated.

Carcinoma

Clear-cell adenocarcinoma associated with DES may occur in either cervix or vagina. Endometroid elements and mixtures of clear-cell and endometroid elements have been described. Available studies concerning prognosis and followup of these patients are few. The Tumor Registry reports that 79% (43 patients) with vaginal carcinoma and 64% (22 patients) with cervical carcinoma are alive two years following treatment.⁵ Radical hysterectomy, vaginectomy, pelvic lymph node dissection and skin grafting have been applied as treatment. X-ray treatment has not proven to be effective.

Prognosis is related to mitotic activity and invasion of lymphatics and lymph nodes. As reported in 1973⁵, seventeen patients had died or developed recurrence in spite of the fact that followup in many instances was less than two years.

Contraception

Inasmuch as the disease is new and followup studies are of short duration, a definite answer concerning the advisability of the use of oral contraceptives in these patients is not available. The weight of evidence at present is that the risk of using oral contraceptives in DES exposed patients is

extremely low. Should pregnancy occur, it appears to have no adverse influence upon adenosis already present.

Followup Examinations

Patients found free of atypical colposcopic findings are followed at yearly intervals with cytologic smears, Schiller's stain, and colposcopy. If benign or atypical colposcopic findings are noted, the patient is seen at three to six month intervals depending upon the degree of anatomical change. Lesions which are symptomatic or reveal nuclear atypicality are treated by local excision. Cautery or cryotherapy is reserved for treating symptomatic cervical ectopy.

References

1. SMITH, O.W.: D.E.S. in Prevention and Treatment of Complications of Pregnancy. *American Journal of Ob/Gyn.* 1948 56, 821-836.
2. HERBST, SCULLY: Adenocarcinoma of Vagina in Adolescence. *Cancer* 1970 25:745-757.
3. HERBST *et al*: Adenocarcinoma of the Vagina. *New England Journal of Medicine* 1971. 284: 878-881.
4. HERBST *et al*: Clear-Cell Adenocarcinoma of Genital Tract in Young Females. *New England of Medicine* 1973. 287:1259-64.
5. A.C.O.G. Technical Bulletin. No 22. May 1973.
6. Ob-Gyn News. News 1, 1973.
7. VON PREUSCHEN F.: Ueber Cystenbildung in der vagina. *Arch Path Anat* 1877. 70:111.
8. PLAUT A. DREYFUSS ML.: Adenosis of Vagina and its relation to primary adenocarcinoma of Vagina. *Surg Gynecol Obstet* 1940. 71:756-765.
9. STAFL, A. *et al*, Ob-Gyn, 1974. Vol 43, #1 p 118.
10. DODDS, E. C., GOLDBERG, L., LAWSON, W., ROBINSON, R.: Ostrogenic Activity of Alkylated Stilbestrols, *Nature, Lond*, 1938, 142:34.
11. Personal interview with Dr. Herbst.

Dr. Marlow, Program Director, Columbia Hospital for Women and Assistant Professor, Department of Obstetrics and Gynecology, George Washington University School of Medicine, Washington, D.C.

Reprint requests may be addressed to Dr. Marlow at Columbia Hospital for Women, Washington, D.C. 20037.

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Woman (man) cannot.

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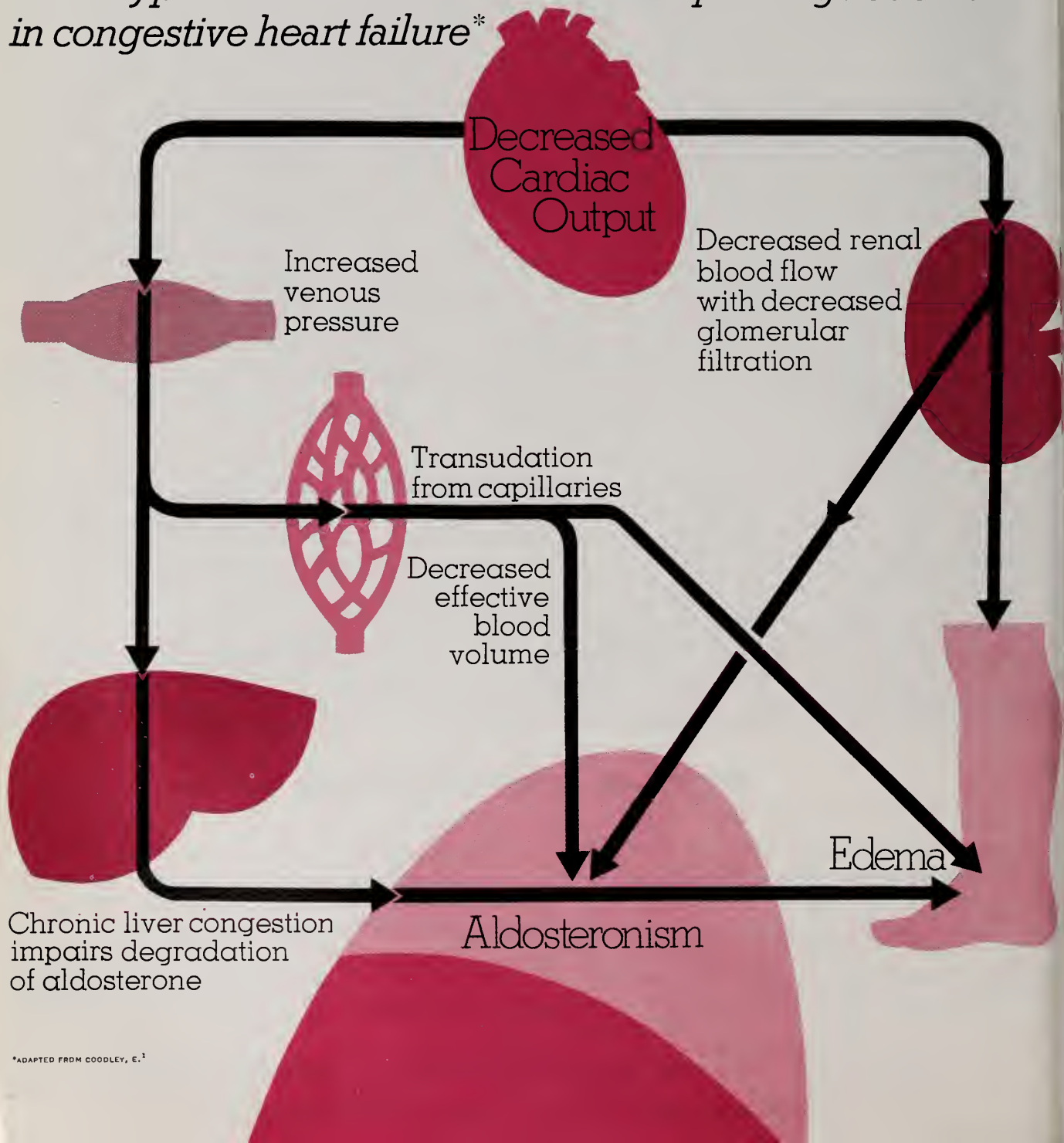
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In congestive heart failure... **secondary aldosteronism**

*How hyperaldosteronism leads to and prolongs edema in congestive heart failure**



is a primary factor

To "switch off" the aldosterone factor in congestive heart failure

Aldactone brand of **spironolactone 25-mg. tablets** *the only specific aldosterone antagonist... basic in all diuretic therapy*

Three ways to use Aldactone in congestive heart failure

- 1. As the only diuretic**
 - Often sufficient alone.
 - Produces gradual, sustained diuresis by blocking aldosterone action in the distal renal tubule.
 - Avoids potassium loss.
- 2. As the basic daily diuretic with an "add-on" alternate-day-diuretic ("A.D.D." schedule)**
 - Can be administered daily as basic therapy with the additional agent (furosemide or ethacrynic acid) given every second or third day.
 - Aldactone plus "A.D.D." schedule minimizes potassium deficiency and potentiates effect of "add-on" diuretic.²
 - Avoids acute volume depletion and aldosterone rebound.²
- 3. As a daily diuretic in combination with a daily dose of a thiazide**
 - Permits daily additive diuretic effect while maintaining potassium balance.

Indications—Essential hypertension; edema or ascites of congestive heart failure, cirrhosis of the liver and the nephrotic syndrome; idiopathic edema. Some patients with malignant effusions may benefit from Aldactone (spironolactone), particularly when given with a thiazide diuretic.

Contraindications—Acute renal insufficiency, rapidly progressing impairment of renal function, anuria and hyperkalemia.

Warnings—Potassium supplementation may cause hyperkalemia and is not indicated unless a glucocorticoid is also given. Discontinue potassium supplementation if hyperkalemia develops. **Usage of any drug in women of childbearing age requires that the potential benefits of the drug be weighed against its possible hazards to the mother and fetus.**

Precautions—Patients should be checked carefully since electrolyte imbalance may occur. Although usually insignificant, hyperkalemia may be serious when renal impairment exists; deaths have occurred. Hyponatremia, manifested by dryness of the mouth, thirst, lethargy and drowsiness, together with a low serum sodium may be caused or aggravated, especially when Aldactone is combined with other diuretics. Elevation of BUN may occur, especially when pretreatment hyperazotemia exists. Mild acidosis may occur. Reduce the dosage of other antihypertensive drugs, particularly the ganglionic blocking agents, by at least 50 percent when adding Aldactone since it may potentiate their action.

Adverse Reactions—Drowsiness, lethargy, headache, diarrhea and other gastrointestinal symptoms, maculopapular or erythematous cutaneous eruptions, urticaria, mental confusion, drug fever, ataxia, gynecomastia, inability to achieve or maintain erection, mild androgenic effects, including hirsutism, irregular menses and deepening voice. Adverse reactions are infrequent and usually reversible.

Dosage and Administration—For essential hypertension in adults the daily dosage is 50 to 100 mg. in divided doses. Aldactone may be combined with a thiazide diuretic if necessary. Continue treatment for two weeks or longer since an adequate response may not occur sooner. Adjust subsequent dosage according to response of patient.

For edema, ascites or effusions in adults initial daily dosage is 100 mg. in divided doses. Continue medication for at least five days to determine diuretic response; add a thiazide or organic mercurial if adequate diuretic response has not occurred. Aldactone dosage should not be changed when other therapy is added. A daily dosage of Aldactone considerably greater than 75 mg. may be given if necessary.

A glucocorticoid, such as 15 to 20 mg. of prednisone daily, may be desirable for patients with extremely resistant edema which does not respond adequately to Aldactone and a conventional diuretic. Observe the usual precautions applicable to glucocorticoid therapy; supplemental potassium will usually be necessary. Such patients frequently have an associated hyponatremia—restriction of fluid intake to 1 liter per day or administration of mannitol or urea may be necessary (these measures are contraindicated in patients with uremia or severely impaired renal function). Mannitol is contraindicated in patients with congestive heart failure, and urea is contraindicated with a history or signs of hepatic coma unless the patient is receiving antibiotics orally to "sterilize" the gastrointestinal tract.

Glucocorticoids should probably be given first to patients with nephrosis since Aldactone, although useful for diuresis, will not directly affect the basic pathologic process.

For children the daily dosage should provide 1.5 mg. of Aldactone per pound of body weight.

References: 1. Coodley, E.: Consultant 12:106-107, 109, 111, 113, 115 (July) 1972. 2. Tharn, G. W., and Lauler, D. P.: Am. J. Med. 53:673-684 (Nov.) 1972.

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The Role of the Detail Man

"I may be prejudiced, but I am very much in favor of the detail men I meet. Most of them are knowledgeable about the drugs they promote and can be a great help in acquainting me with new medication."

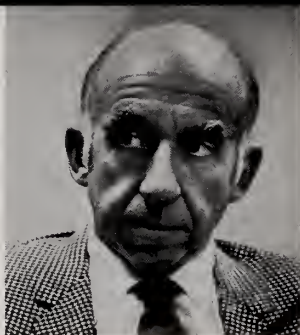
Family Physician's Perception

I think that most general practitioners in this area feel as I do about the detail man. Over the years I have gotten to know most of the men who visit me regularly and they in turn have become aware of my particular interests and the nature of my practice. They, therefore, limit their discussion as much as possible to the areas of interest to me. Since I usually see the same representative again in future visits, it is in his best interest to supply me with the most honest, factual, as well as up-to-date information about his products.



Dr. Willard Gobbell
Family Physician
Encino, California

Dr. Jeremiah Stamler
Chairman,
Department of Community
Health and Preventive
Medicine, and Dingman
Professor of Cardiology
Northwestern University
Medical School



"In the total picture of dealing with health problems in this country, there is a potential for detail men to play a meaningful role."

The Positive Influence

My contact with representatives and salesmen of the pharmaceutical industry is the type of contact that people in a medical center, research people, and academic people have and that's in all likelihood on a somewhat different level from that of the practicing physician.

Let me touch on how I personally perceive the role of the sales representative. These men reach large numbers of health professionals. Thus they could be—and at times actually are—disseminators of useful information. They could consistently serve a real educational function in their ability to discuss their products.

At present they do distribute printed material, brochures and pamphlets—some of it scientifically sound and therefore truly useful—as well as some excellent films produced by the pharmaceutical industry. When they function in this

Opinion
&
Dialogue

Is He a Source of Information?

Yes, with certain reservations. The average sales representative has a great fund of information about the drug products he is responsible for. He is usually able to answer most questions fully and intelligently. He can also supply reprints of articles that contain a great deal of information. Here, too, I exercise some caution. I usually accept most of the statements and opinions that I find in the papers and studies which come from the larger teaching facilities. It goes without saying that a physician should also rely on other sources for his information on pharmacology.

Training of Sales Representatives

Ideally, a candidate for the position as a sales representative of a pharmaceutical company should be a graduate pharmacist who has a questioning mind. I don't think this is possible in every case, and so it becomes the responsibility

of the pharmaceutical company to train these individuals comprehensively. It is of very great importance that the detail man's knowledge of the product he represents be constantly reviewed as well as updated. This phase of the sales representative's education should be a major responsibility of the medical department of the pharmaceutical company.

I am certain that most of these companies take special care to give their detail men a great deal of information about the products they produce—information about indications, contraindications, side effects and precautions. Yet, although most of the detail men are well informed, some, unfortunately, are not. It might be helpful if sales representatives were reassessed every few years to determine whether or not they are able to fulfill their important function. Incidentally, I feel the same way about periodic assessments of everyone

in the health care field, whether they be general practitioners, surgeons or salesmen.

Value of Sampling

I personally am in favor of limited sampling. I do not use sampling in order to perform clinical testing of a drug. I feel that drug testing should rightly be left to the pharmacology researcher and to the large teaching institutions where such testing can be done in a controlled environment.

I do not use samples as a "starter dose" for my patients. I do, however, find samples of drugs to be of value in that they permit me to see what the particular medication looks like. I get to see the various forms of the particular medication at first hand, and if it is in a liquid form I take the time to taste it. In that way I am able to give my patients more complete information about the particular medications that I prescribe for them.

capacity they are indeed useful; particularly in the fact that they disseminate broadly based educational material and serve not just as "pushers" of their drugs.

The Other Side of the Coin

Obviously, the pharmaceutical companies are not producing all this material as a labor of love—they are in the business of selling products for profit. In this regard the ambitious and improperly motivated sales representative can exert a negative influence on the practicing physician, both by presenting a one-sided picture of his product, and by encouraging the practitioner to depend too heavily on drugs for his total therapy. In these ways, the salesman has often distorted objective reality and undermined his potential role as an educator.

The Industry Responsibility

Since the detail man must be an information resource as well as a representative of his particular pharmaceutical company, he should be carefully selected and

thoroughly trained. That training, perforce, must be an ongoing one. There must be a continuing battle within and with the pharmaceutical industry for high quality not only in the selection and training of its sales representatives, but also in the development of all of its promotional and educational material.

The industry must be ready to accept constructive as well as corrective criticism from experts in the field and consumer spokesmen, and be willing to accept independent peer review. The better educated and prepared the salesman is, the more medically accurate his materials, the better off the pharmaceutical industry, health professionals and the public—i.e., the patients—will be.

Physician Responsibility

The practicing physician is in constant need of up-dated information on therapeutics, including drugs. He should and does make use of drug information and answers to specific questions supplied by the pharmaceutical representative. However, that informa-

tion must not be his main source of continuing education. The practitioner must keep up with what is current by making use of scientific journals, refresher courses, and information received at scientific meetings.

The practicing physician not only has the right, but has the responsibility to demand that the pharmaceutical company and its representatives supply a high level of valid and useful information. I feel certain that if such a high level is demanded by the physician as well as the public, this demand will be met by an alert and concerned pharmaceutical industry.

From my experience, my impression is that sectors of the pharmaceutical industry are indeed ethical. I challenge the industry as a whole to live up to that word in its finest sense.

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Sidonna. The therapeutic partnership approach to functional or organic GI disturbances including spastic colon, irritable bowel syndrome, gastroenteritis, gastritis, peptic ulcer and nervous indigestion.

Contraindications: hypersensitivity to barbiturates or belladonna alkaloids; glaucoma, prostatic hypertrophy, pyloric obstruction. **Side Effects:** dry mouth, blurred vision, dysuria, skin rash, constipation or drowsiness. **Dosage:** one or two tablets preferably before meals and at bedtime.

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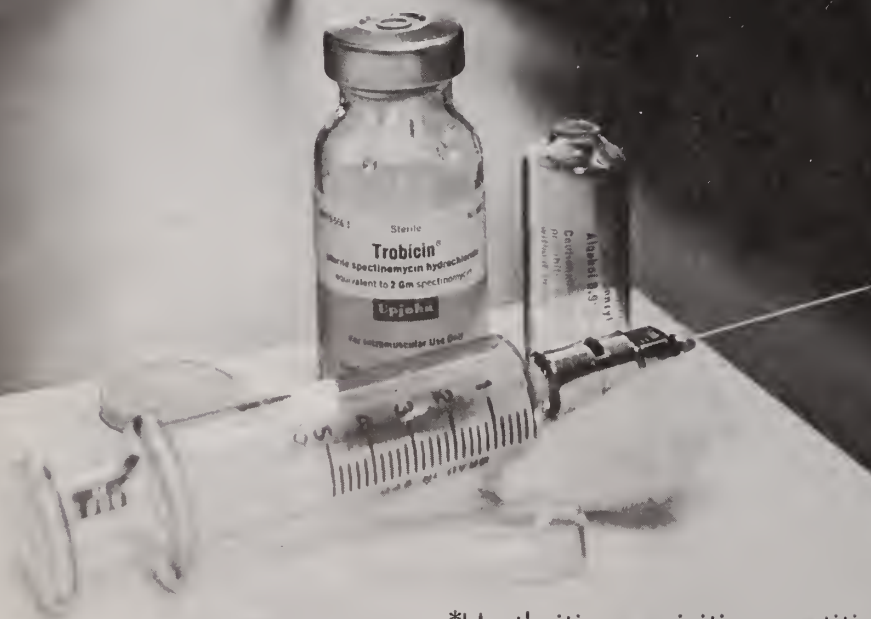
Each scored tablet contains: specially activated simethicone 25 mg., hyoscyamine sulfate 0.1037 mg., atropine sulfate 0.0194 mg., hyoscine hydrobromide 0.0065 mg. (equivalent to belladonna alkaloids [as bases] 0.1049 mg.) and butabarbital sodium N.F. 16 mg. (Warning: may be habit forming.)

**A working partnership
against the
pain of gas and spasm**

acute gonorrhea

This patient
just received
an effective, private,
physician-controlled
treatment.

It took just one short visit...



*Urethritis, cervicitis, proctitis when due
to susceptible strains of *N. gonorrhoeae*

Trobicin—The advantage of injectable therapy.

Once Trobicin is injected, treatment is usually complete; there can be no problems with patients sharing, skimping, skipping or forgetting medication.

Trobicin—The aspect of privacy.

There are no prescriptions to fill, no capsules to take. Neither family, friends nor co-workers need know or suspect the patient's problem.

Trobicin—Indication and dosage.

Spectinomycin is indicated only for use in acute urethritis and proctitis in the male and acute cervicitis and/or proctitis in the female when due to susceptible strains of *N. gonorrhoeae*. The usual dosage for Trobicin in adult males is 2 grams intramuscularly[†]; 4 grams intramuscularly in females.

Trobicin—Not effective for syphilis.

Trobicin is not effective for any stage of syphilis. Trobicin may mask or delay the symptoms of incubating syphilis. If concurrent syphilis is suspected, follow the patient serologically for at least 3 months. Patients with syphilis should receive adequate specific anti-syphilitic therapy with an appropriate antibiotic.

Trobicin is contraindicated in patients previously found hypersensitive to it.

Intramuscular

...and **Trobicin**[®] 2 gm and 4 gm vials sterile spectinomycin hydrochloride

Sterile Trobicin

Sterile Trobicin (spectinomycin hydrochloride)
— For Intramuscular Injection:

2 gm vials containing 5 ml when reconstituted with diluent.

4 gm vials containing 10 ml when reconstituted with diluent.

An aminocyclitol antibiotic active *in vitro* against most strains of *Neisseria gonorrhoeae* (MIC 7.5 to 20 mcg/ml). Definitive *in vitro* studies have shown no cross resistance of *N. gonorrhoeae* between spectinomycin and penicillin.

Indications: Acute gonorrheal urethritis and proctitis in the male and acute gonorrheal cervicitis and proctitis in the female when due to susceptible strains of *N. gonorrhoeae*.

Contraindications: Contraindicated in patients previously found hypersensitive to spectinomycin.

Warnings: Not indicated for the treatment of syphilis. Antibiotics used to treat gonorrhea may mask or delay the symptoms of incubating syphilis. Patients should be carefully examined and monthly serological follow-up for at least 3 months should be instituted if the diagnosis of

syphilis is suspected.

Safety for use in infants, children and pregnant women has not been established.

Precautions: The usual precautions should be observed with atopic individuals.

Clinical effectiveness should be monitored to detect evidence of development of resistance by *N. gonorrhoeae*.

Adverse reactions: The following reactions were observed during the single-dose clinical trials: soreness at the injection site, urticaria, dizziness, nausea, chills, fever and insomnia. During multiple-dose subchronic tolerance studies in normal human volunteers, the following were noted: a decrease in hemoglobin, hematocrit and creatinine clearance; elevation of alkaline phosphatase, BUN and SGPT. In single- and multiple-dose studies in normal volunteers, a reduction in urine output was noted. Extensive renal function studies demonstrated no consistent changes indicative of renal toxicity.

Dosage and administration: Keep at 25° C and use within 24 hours after reconstitution with diluent.

Male—Inject 5 ml intramuscularly for a 2 gram dose. Patients with gonorrheal proctitis and patients being re-treated after failure of previous antibiotic therapy should receive 4 grams (10 ml). In geographic areas where antibiotic resistance is known to be prevalent, initial treatment with 4 grams (10 ml) intramuscularly is preferred.

Female—Inject 10 ml intramuscularly for a 4 gram dose.

How supplied: Vials, 2 and 4 grams—with ampoule of Bocteroistotic Water for Injection with Benzyl Alcohol 0.9% w/v. Reconstitution yields 5 and 10 ml respectively with a concentration of 400 mg spectinomycin per ml (as the hydrochloride). For intramuscular use only. **Susceptibility Powder**—for testing *in vitro* susceptibility of *N. gonorrhoeae*.

Caution: Federal law prohibits dispensing without prescription.

For additional product information see your Upjohn representative or consult the package insert.

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MED B-5-5 (MBR-1)

[†]For patients with gonorrheal proctitis and for patients in geographic areas where antibiotic resistance is known to be prevalent, initial treatment with 4 grams is preferred.



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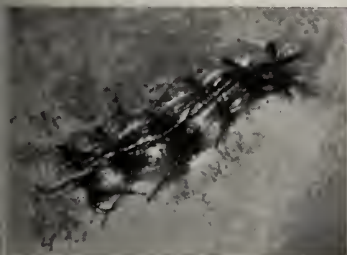
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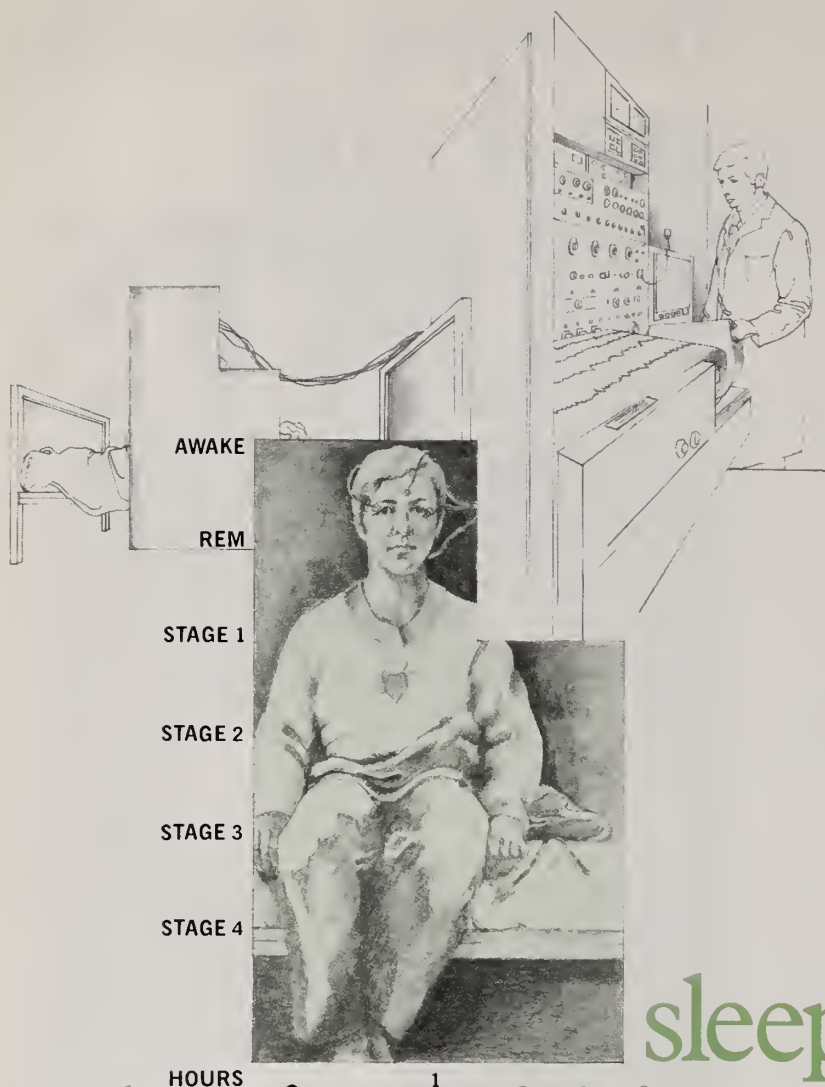


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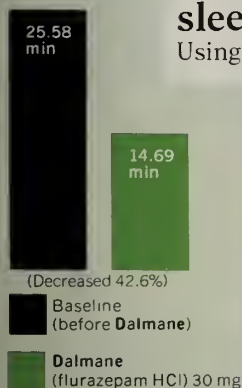


sleep
begins within
17 minutes, on average ...
an initial benefit of

Dalmane[®]
(flurazepam HCl) proved by a
22-night clinical study of insomnia patients
in the sleep research laboratory and at home¹

Three insomnia patients selected for difficulty falling asleep were administered Dalmane (flurazepam HCl) 30 mg for 14 consecutive nights. Placebo was given for four nights prior to and four nights after Dalmane. Physiologic tracings on Dalmane nights 1-3 showed sleep induction time averaged 13.90 minutes; on Dalmane nights 12-14, 18.80 minutes. Combined average for the 6 monitored drug nights was 16.35 minutes.¹

Average Time Required
to Fall Asleep (4 Studies,
16 Subjects²⁻⁵)



confirmed by clinical studies in four geographically separated sleep research laboratories²⁻⁵

Using a 14-night protocol involving eight insomniac and eight normal subjects, four studies confirmed the sleep-inducing effectiveness of Dalmane (flurazepam HCl) and the reproducibility of this response. On average, one 30-mg capsule induced sleep within 17 minutes. In all these studies, Dalmane induced sleep rapidly, reduced nighttime awakenings, and provided 7 to 8 hours of sleep without repeating dosage²⁻⁵

Dalmane (flurazepam HCl) induces and maintains sleep, with relative safety

Dalmane is generally well tolerated; morning "hang-over" has been relatively infrequent. While dizziness, drowsiness, lightheadedness and the like have been noted most often, particularly in the elderly and debilitated, physicians should be aware of the possibility of more serious reactions, as noted below.

Before prescribing Dalmane (flurazepam HCl), please consult Complete Product Information, a summary of which follows:

Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening; in patients with recurring insomnia or poor sleeping habits; and in acute or chronic medical situations requiring restful sleep. Since insomnia is often transient and intermittent, prolonged administration is generally not necessary or recommended.

Contraindications: Known hypersensitivity to flurazepam HCl.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Use in women who are or may become pregnant only when potential benefits have been weighed against possible hazards. Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated, initial dosage should be limited to 15 mg to preclude oversedation, dizziness and/or ataxia. If combined with other drugs having hypnotic or CNS-depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with latent depression or suicidal tendencies. Periodic blood counts and liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdose, have been reported. Also reported were headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins and alkaline phosphatase. Paradoxical reactions, e.g., excitement, stimulation and hyperactivity, have also been reported in rare instances.

Dosage: Individualize for maximum beneficial effect. *Adults:* 30 mg usual dosage; 15 mg may suffice in some patients. *Elderly or debilitated patients:* 15 mg initially until response is determined.

Supplied: Capsules containing 15 mg or 30 mg flurazepam HCl.

REFERENCES: 1. Kales A, et al: *Arch Gen Psychiatry* 23:226-232, Sep 1970

2. Karacan I, Williams RL, Smith JR: The sleep laboratory in the investigation of sleep and sleep disturbances. Scientific exhibit at the 124th annual meeting of the American Psychiatric Association, Washington DC, May 3-7, 1971

3. Frost JD Jr: Data on file, Medical Department, Hoffmann-La Roche Inc, Nutley NJ

4. Vogel GW: Data on file, Medical Department, Hoffmann-La Roche Inc, Nutley NJ

5. Dement WC: Data on file, Medical Department, Hoffmann-La Roche Inc, Nutley NJ

when restful sleep
is indicated

Dalmane[®]

(flurazepam HCl)

One 30-mg capsule h.s. — usual adult dosage
(15 mg may suffice in some patients).

One 15-mg capsule h.s. — initial dosage for
elderly or debilitated patients.

- induces sleep within 17 minutes, on average
- reduces nighttime awakenings
- sustains sleep 7 to 8 hours, on average, without repeating dosage



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Before prescribing, see complete prescribing information in SK&F literature or *PDR*. The following is a brief summary.

Indications: Edema associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. Also, mild to moderate hypertension.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (> 5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities.

Accordingly, check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently — both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Anti-hypertensive effects may be enhanced in post-sympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Rarely, necrotizing vasculitis, paresthesias, icterus, pancreatitis, and xanthopsia have occurred with thiazides alone.

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*E.D. Freis: The Modern Management of Hypertension, V.A. Information Bulletin, 11-35.

TO KEEP BLOOD PRESSURE DOWN AND KEEP POTASSIUM LEVELS UP

BOOK REVIEWS

Patterns in Forcible Rape. MENACHEM AMIR.
Price, \$15.00. Pp. 394. Chicago, Illinois: Univ. of
Chicago Press, 1971.

Rape is the most under-reported crime in the nation which should not surprise anyone considering the false impressions many people have about women who get raped. But, Amir, Head of the Research Department in the Ministry of Social Welfare in Israel, takes us past stereotypes and presents us with a well organized statistical analysis of this crime which refutes many of our widely held beliefs.

The basis for his book comes from his study of 646 reported rape cases in the police files of Philadelphia that occurred in the years 1958 and 1960. And while other studies on rape have concentrated either on single case histories of the sex offender and his victim or general surveys of sex offenses, no other work has, in this reviewer's opinion, been able to match the monumental effort presented by Amir—dispassionate, scholarly and overwhelming in its systematic analysis of the factors involved in the exploitation by one individual of another. Though the basis for this study is more than a decade old, it loses none of its impact and freshness. Rape is not so much a sexual act as it is a violent crime with the purpose of humiliating and degrading the victim the primary aim. By society's less than empathetic identification with the suffering victim, we act to perpetuate her humiliation and shame and "punish" her more.

But, what makes a man a rapist and what kind of female gets assaulted? Amir, though relying on data borrowed from psychiatric literature on the individual dynamics of sex offenders and their victims, brings this crime into still sharper focus by exposing the sociocultural factors that influence the individual's decision to commit rape. His study reduces the phenomena of rape to its objective characteristics appearing regularly and uniformly establishing specific patterns to the offense. He shows, for example, how factors, such as the place where the rape occurs, influence the manner in which the act is carried out, the amount of force used and the extent of sexual humiliation to the victim. He enriches our understanding of psychological motivation through his pointing out the important relationships that exist between the sociological variables involved in the decision to rape. Variables such as the site of the crime, the victim-offender relationship, especially in child assault cases, the degree of violence the victim is subjected to, the racial patterns, the seasonal variation, the impact of

alcohol on the crime and relates these and other variables to each other so as to make the reader aware of recognizable patterns that emerge in the commission of this offense.

I could not accept every theoretical position reached by Amir, such as his positing the existence of a subculture of aggression and violence without some disclaimer. But, as a phenomenological study of rape, his book stands as a classic in its field, frequently referred to and acknowledged by all serious investigators of the crime of sexual assault. His bibliography alone runs more than twenty-nine pages and stands as a small index medicus on sexual aggression.

This book should appeal to those who are concerned with the rising incidence of aggression and violence committed by individuals so as to gain an understanding of the sociocultural and psychological factors involved. It is important for us to know these things because, to paraphrase Nietzsche, if man can find a *why* something occurs, he can also find a *how* to prevent it.

EDWARD H. WEISS, M.D.

Ureteral Dynamics, Pathophysiology, Drugs and Surgical Implications. SAUL BOYARSKY, M.D.
AND PEREGRINA LABAY, M.D. Price \$18.50. Pp.
493. Baltimore, Maryland: Williams & Wilkins
Company, 1972.

This book represents the work on ureteral research started first at Albert Einstein College of Medicine and then at Duke University. It is basically an extension and expansion of that begun in the fifties by the father of Urodynamics, Dr. David M. Davis. Histochemistry, Biochemical Microbiology, Catecholamine Biochemistry, Pharmacology and Radiology are included in this volume in nine well-written chapters where there is progress in the redefinition of pathophysiologic events into basic scientific explanations with a new enriched concept of the ureter being more than a tube or a conduit, even more than a peristaltic organ: it is an adaptive biological system.

Emphasis is placed on the concept of ureteral function influenced by extra-urinary, somatic and nervous diseases. Most of its concepts developed by extensive research are not of practical use because the book is not intended as a guide to treatment, rather it is intended to develop conscience for more urologic experimentation. New concepts and new language are

BOOK REVIEWS

offered for the urologic investigator. Several abbreviated protocols are quoted to present primary evidence for review by future readers to draw their own conclusions. The reader who is not interested in these details can always be referred to the discussion and conclusions.

The chapter on endocrine influences on ureteral function tried to explain the unanswered cause in humans of the Hydronephrosis of Pregnancy and their experience with pregnant dogs leads them to emphasize the mechanical factor.

Special attention is drawn to the microsurgery of the ureter. This technique promises to be useful for

dealing with small ureters such as those of pediatric patients and encourages its use more widely clinically, particularly with the simplified techniques described in the book.

Many interesting questions are raised and left unanswered for new research approaches and directions.

In summary this book is quite a useful addition to the urological literature and should appeal to researchers and maybe now, in much less degree, to the clinician.

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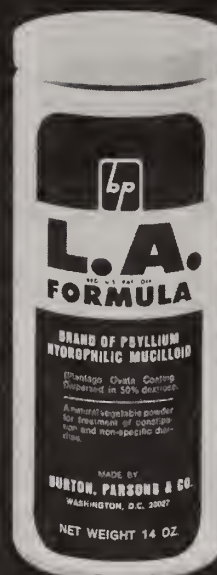


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THE VIEW BOX

(from page 496)

DIAGNOSIS: Amebiasis

Barium Enema examination demonstrates numerous small, superficial mucosal ulcerations involving predominantly the descending and transverse portion of the colon. Also noted was considerable thickening of the bowel wall of the descending colon. There was no radiological involvement of rectum, cecum or distal small bowel.

The primary diagnostic possibilities are those of ulcerative colitis and parasitic involvement of the colon, particularly amebiasis. The presence of a polypoid mass most frequently seen in the cecum favors a diagnosis of amebiasis but is also seen in tuberculous colitis or actinomycosis of the cecum. In the absence of mass defect, amebiasis and ulcerative colitis are indistinguishable by x-ray findings. This lady was from Argentina and subsequent Entamoebic Histolytica were recovered from stool specimens.

*Edited by Gunther J. Augustin, M.D.
Senior Attending Radiologist, Washington
Hospital Center, Washington, D.C.*

ECG PROBLEMS

(from page 502)

INTERPRETATION:

1. Pacemaker is firing continuously (the magnet cancels the inhibitory function of the pulse generator.)
2. Spike-to-spike intervals are 0.86 seconds with a resultant rate of 70 per minute.
3. The pacemaker captures and drives the ventricles whenever it fires during a non-refractory period.
4. Inhibition of the pacemaker by the patient's own ventricular complexes was demonstrated to have been appropriate. The patient's own rate was rapid enough and inhibition was complete enough that the magnet needed to be used in order to make the pulse generator fire.

Note the pacemaker artifact in the T wave of the first complex in the top strip and the fourth complex of the bottom strip. In these two instances the pacemaker fired at the apex of the T wave. This is the so-called vulnerable zone. Delivery of an electrical impulse at this portion of the cardiac cycle is capable of causing repetitive firing or even a sustained ventricular arrhythmia. The observations in this case, however, demonstrate that such an impulse delivered at such a time does not necessarily produce repetitive or sustained rhythm disturbance. The vulnerability of that phase of the cardiac cycle may be accentuated by anoxia or acid base imbalance. This may explain why an impulse delivered at such a time when the patient has acute myocardial infarction is more likely to produce sustained ventricular arrhythmia.

*Edited by
Robert R. Montgomery, M.D.*

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Information to Authors of Manuscripts Submitted to The Medical Annals of the District of Columbia

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The number of references should not exceed 18 single complete bibliographic citations, except in Special Articles.

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lications of Cardiac Pacemakers,
Medical Annals of D.C., 1973, 42,
165.

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Use generic or descriptive names of drugs when available. Trade names, capitalized, may be given in parentheses when the drug is first mentioned.

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Laboratory data should not be given in abbreviated form but in full (e.g., "hemoglobin level, 12 Gm. per 100 ml." rather than "Hb. 12 GM.%").

Figures should be used for number 10 and above, laboratory measurements, percentages, and ages.

Metric equivalents should be given for dosage and body height and weight.

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Do not attach paper clips or cellophane tape to photographs.

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District of Columbia Manpower Administration	T-531
Nutrition Education	
Dairy Council of Greater Metropolitan Washington, D.C.	2
Pharmaceuticals	
Abbott Laboratories	T-507
Burroughs Wellcome & Company	T-521
Burton, Parsons & Company, Inc.	
Dorsey Laboratories	T-512, T-517
Eli Lilly & Company	8
McNeil Laboratories	7
Pharmaceutical Manufacturers Association	
Reed & Carnrick	T-510, T-511
A. H. Robins Company	T-513
Roche Laboratories	T519-520
G. D. Searle & Company	C2, 1, C3, C4
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Upjohn Company	T-524
	T-514-T515
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Precautions: Use cautiously in patients with impaired renal or hepatic function, possible folate deficiency, allergy or bronchial asthma; and in those with glucose-6-phosphate dehydrogenase deficiency, where hemolysis may occur. During therapy, maintain adequate fluid intake and perform frequent urinalyses, with careful microscopic examination, and renal function tests, particularly where there is impaired renal function.

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exfoliative dermatitis, anaphylactoid reactions, peri-orbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. *Gastrointestinal reactions:* Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis. *CNS reactions:* Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. *Miscellaneous reactions:* Drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L.E. phenomenon. Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia in patients; cross-sensitivity with these agents may exist. In rats, long-term therapy with sulfonamides has produced thyroid malignancies.

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neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive dis-

orders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anti-convulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful

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According to her major symptoms, she is a psychoneurotic patient with severe anxiety. But according to the description she gives of her feelings, part of the problem may sound like depression. This is because her problem, although primarily one of excessive anxiety, is often accompanied by depressive symptomatology. Valium (diazepam) can provide relief for both—as the excessive anxiety is relieved, the depressive symptoms associated with it are also often relieved.

There are other advantages in using Valium for the management of psychoneurotic anxiety with secondary depressive symptoms: the psychotherapeutic effect of Valium is pronounced and rapid. This means that improvement is usually apparent in the patient within a few days rather than in a week or

two, although it may take longer in some patients. In addition, Valium (diazepam) is generally well tolerated; as with most CNS-acting agents, caution patients against hazardous occupations requiring complete mental alertness.

Also, because the psychoneurotic patient's symptoms are often intensified at bedtime, Valium can offer an additional benefit. An *h.s.* dose added to the *b.i.d.* or *t.i.d.* treatment regimen can relieve the excessive anxiety and associated depressive symptoms and thus encourage a more restful night's sleep.

For further information on this subject, the following references are provided:

1. Henry BW, *et al*: *Dis Nerv Syst* 30:675-679, Oct 1969.
2. Hollister LE, *et al*: *Arch Gen Psychiatry* 24:273-278, Mar 1971.
3. Claghorn J: *Psychosomatics* 11:438-441, Sept-Oct 1970.

surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of child-bearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies.

Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or over-sedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle

spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.



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The statement also affirms the advisability of using milk as an excellent source of protein in child feeding programs.

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CONTENTS

SCIENTIFIC ARTICLES

Benign Recurrent Cholestasis: A Manifestation of Pancreatitis. Fernando A. Salazar, M.D., Bernard A. Heckman, M.D., William O. Dobbins, III, M.D. and Stuart H. Danovitch, M.D. . . .	533
Hepatic Artery-Portal Vein Fistula with Hepatic Cirrhosis, Hepatoma and Bleeding Esophageal Varices. Louis T. Kanda, M.D., Luis A. Mispireta, M.D., Joseph P. Mock, M.D. and Karel B. Absolon, M.D. . . .	543
Primary Linitis Plastica Carcinoma of the Colon. Tali Bashour, M.D., Milton L. Goldman, M.D., Leon Gerber, M.D. and Stuart H. Danovitch, M.D. . . .	549
Syncope Associated with Esophageal Stricture. Nelson P. Trujillo, M.D., and Charles Spero . . .	553

OTHER FEATURES

Editorial	7
Office Hemorrhoidectomy (Elastic Band Ligation). John Joseph O'Connor, M.D. . . .	
Editorial	8
Hepatitis and the Need for Reporting. D.C. Department of Human Resources.	
Scientific Editorial	9
Australia Antigen (HB_sAg). Allen L. Ginsberg, M.D. . . .	
Book Reviews	577
Allergy Management in Clinical Practice. (Tuft) Reviewed by Isaac Weiszer, M.D. . . .	
The Newborn Chest. (Wesenberg) Reviewed by William H. Weinbraub, M.D. . . .	
The View Box	542
Edited by Gunter J. Augustin, M.D. . . .	
ECG Problems	575
Edited by Robert F. Montgomery, M.D. . . .	
Information for Authors	584
Advertising and Subscription Information	586
Index to Advertisers	586



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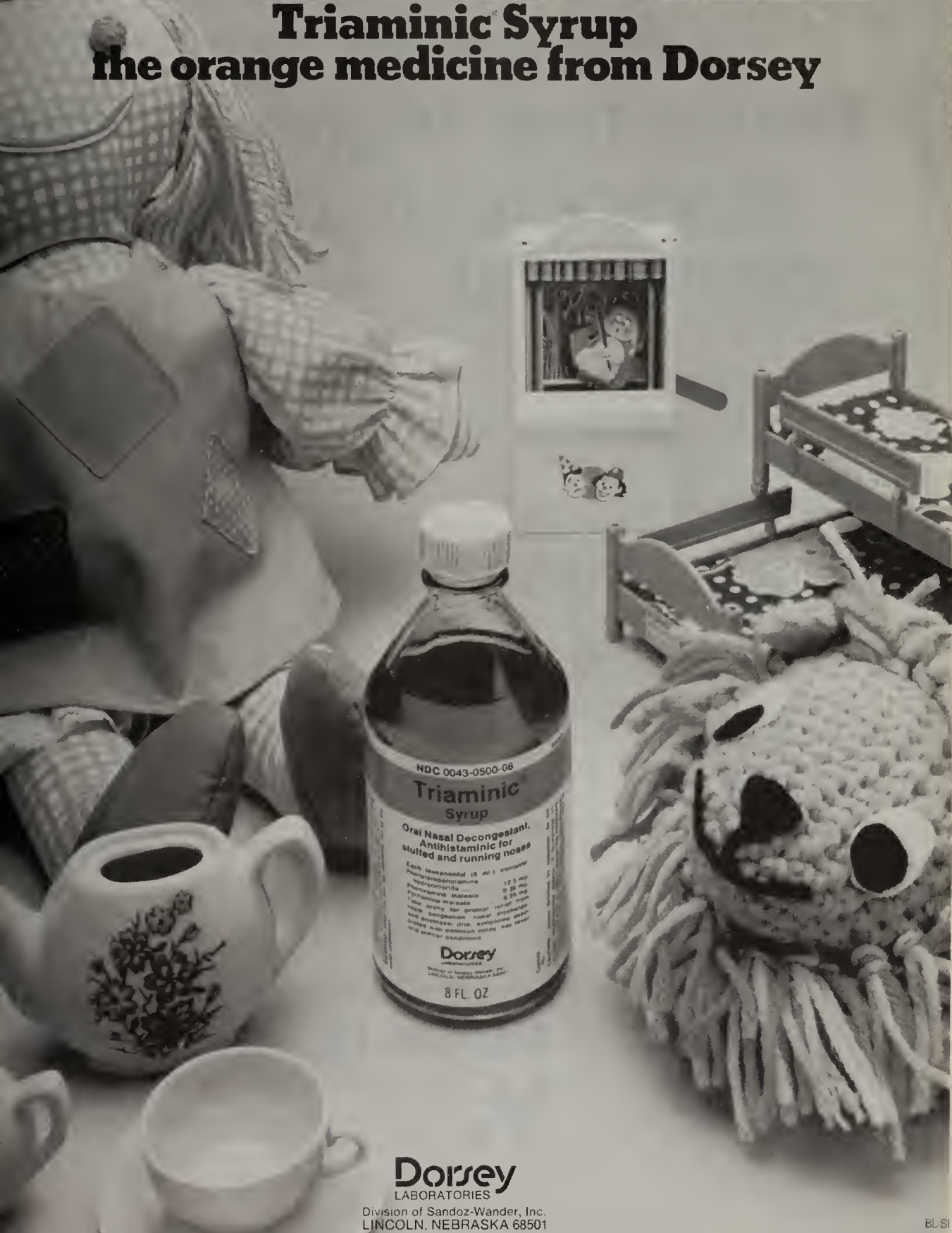


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Editorial

OFFICE HEMORRHOIDECTOMY (Elastic Band Ligation)

JOHN JOSEPH O'CONNOR, M.D.

As with many diseases when numerous forms of therapy are available, the implication is that no specific form of therapy is universally applicable. The treatment of hemorrhoidal disease is no exception.

Hemorrhoidectomy has long been regarded by patients as an unsatisfactory solution. Surgeons are the first to admit it is often fraught with postoperative problems, not the least of which is pain. This probably accounts for the reason so few surgeons undergo hemorrhoidectomy.¹

Because hemorrhoidectomy is an elective procedure, the needs of the patient and his family and economic loss must be considered. It is clear that the period of hospitalization and convalescence attendant upon hemorrhoidectomy is difficult to justify.

Since 1954, an instrument for the out-patient ligation of hemorrhoids has been available.² This has been modified by Barron, and later McGivney, to give better and more predictable results.^{3,4} Because of the excellent results reported, and the initial apparent success in the use of the technique, one hundred patients complaining of hemorrhoidal disease and treated by elastic band ligation (EBL) were reviewed.

Methods and Material

One hundred patients who had symptomatic hemorrhoids, without evidence of associated anorectal disease such as fissures, fistula or external hematomas, were treated by EBL. Symptoms included bleeding, prolapse, pain, and discharge or soiling. Large skin tags and hypertrophied anal papillae were not treated by ligation.

As with any patient considered to have anorectal disease, a complete history is taken and physical examination is performed. Anoscopy, sigmoidoscopy, and where appropriate, barium enema are performed.

The nature of the treatment, as explained to the patient, represents an internal hemorrhoidectomy. It

is further explained that it may require from one to four visits to accomplish eradication of the hemorrhoids. The patient is further told to expect a sense of rectal fullness for approximately twelve hours, but that this will not interfere with work or normal activity.

The hemorrhoids are visualized through the anoscope, and ligations are performed in the usual hemorrhoidal areas (right anterior, right posterior and left lateral positions). The hemorrhoid is prolapsed through the drum of the ligator and the ligation is accomplished by release of the band onto the hemorrhoid. Up to three bandings can be accomplished without patient discomfort.

Upon completing the procedure, the patient is told to eat a regular diet, to use mineral oil if stools become hard, and to take a sitz bath daily if there is discomfort. Activity is not restricted, and all patients return to normal activity the day of ligation. When the hemorrhoid sloughs in 72-96 hours, spotting of blood may be noted.

Reevaluation is carried out in three weeks and additional ligations are performed, if necessary.

Results

Complications following ligation have been reported. They include bleeding, severe pain, and external thrombosis and ulceration. Of the one hundred patients treated, excessive bleeding necessitating ice lavage the rectal ampula occurred only once. There were no cases of pain requiring medication. External thrombosis and anal ulceration were likewise not seen.

All patients experienced relief of their symptoms and were pleased with the results. With the exception of the one bleeding episode, there was no time loss from work. Four patients, upon anoscopic examination, have residual disease after three ligations, but are asymptomatic.

References

1. CORMAN, M. L. and VEIDENHEIMER, M. C.: The New Hemorrhoidectomy. Symposium on Surgical Techniques. Surgery Clinics North America. 53, 417-422, 1973.
2. BLAISDELL, P. C.: Scientific Exhibit, AMA. San Francisco, June 1954.
3. BARRON, J.: Office Ligation of Internal Hemorrhoids. American Journal of Surgery. 105: 563-570, 1963.
4. MCGIVNEY, J. Q.: The Ligation Treatment of Internal Hemorrhoids—A Two Year Experience. Texas State Journal of Medicine (in press).

HEPATITIS AND THE NEED FOR REPORTING

The reporting of communicable diseases remains an intricate issue. One uniform mechanism for reporting, instituted by local, district, county or state health departments, might prove successful for some diseases while yielding little information with others. This is due in part to the fact that different institutions in the medical community respond by reporting communicable diseases at a different rate. Data from the Center for Disease Control in Atlanta indicate that for outbreaks of hepatitis (types A and B), the percent of hospitalized persons with hepatitis to the total number of persons found to have hepatitis ranged from 15 to 40%, leaving the vast majority to be seen and diagnosed by private physicians and outpatient facilities.

It is easy to observe that with hepatitis A over 90% of cases reported were hospitalized cases reported by infection control practitioners in the respective hospitals. In fact, not one case was reported by a private physician. For hepatitis B, the overwhelming majority again were reported from hospitalized cases and the hospitals' Infection Control practitioners. While a respectable percent come from Red Cross information, few are reported by private physicians.

We are sure that the majority of hospitalized cases of patients with hepatitis A, B and unspecified are

reported, and if we do not have on record every hospitalized case, the data we do have from hospitals are representatives of hospitalized cases of hepatitis in this city. However, realizing that 85 to 60% of cases in epidemics are diagnosed and treated on an outpatient basis by private physicians and house staff in outpatient departments, the poor representation of private physicians in the District of Columbia in reporting hepatitis raises a question as to whether the monthly totals and cumulative totals are accurate.

We would like to strongly urge private physicians to report all cases of hepatitis A (infectious), hepatitis B (serum), and unspecified hepatitis to [Communicable Disease Control Branch of the Department of Human Resources, Suite 815, 1875 Connecticut Avenue, N.W., Washington, D.C. This may be done by submitting one of the disease case report cards,] [or by calling the office at 629-3093 or 629-3640.]

DISEASE CASE REPORT *			
DISEASE *		DATE OF REPORT *	DATE OF ONSET
PATIENT'S NAME		AGE	SEX RACE
HOME ADDRESS		TELEPHONE NO.	
LOCATION OF CASE		DATE ADMITTED TO HOSPITAL	
NAME OF SCHOOL OR PLACE OF EMPLOYMENT			
Were proper persons instructed as required by Subsection 8-5105(a) of the Regulations? If not, set forth in detail on an additional sheet.			
NAME OF LABORATORY			
NAME OF PERSON IN CHARGE OF CASE			
ADDRESS		TELEPHONE NO.	

SCIENTIFIC Editorial

AUSTRALIA ANTIGEN (HBsAg)

ALLEN L. GINSBERG, M.D. Assistant Professor of
Medicine George Washington University School of
Medicine

The discovery by Blumberg of an antigen in the blood of patients infected with Hepatitis B represents a major breakthrough in hepatitis research.¹ His observation of a precipitin reaction between serum from a multiply transfused hemophiliac and serum from an Australian Aborigine was destined to have far reaching effects. This observation was initially thought to represent a reaction of an antibody in the hemophiliac serum with a genetically determined serum lipoprotein. This theory was supported by the observation that up to 10% of certain Micronesian populations had the antigen in their sera whereas it could be found in the sera of only 0.1% of residents of the United States. Subsequently, high percentages of sera from patients with leukemia, lepromatous leprosy, Downs Syndrome, and polyarteritis nodosa have been reported to be positive. In retrospect, it is now apparent that these individuals were chronic carriers of the Hepatitis B Virus, and that this chronic carrier state was probably a result of defective cellular immunity.²

Hepatitis B Antigen is an ether sensitive, heat stable (56 degrees/1 hour) lipoprotein with a molecular weight of approximately 2.4 million.³ When purified antigen preparations are examined under the electron microscope three forms of particles are encountered: spherical particles 200 Å in diameter, rod shaped particles 200 Å in diameter and large spherical 420 Å particles (DANE Particles) which seem to have a central core 270 Å in diameter.^{4,5} The Dane particles are considered to be complete virus particles. Spherical and rod shaped forms which are more numerous may only represent outer lipoprotein viral capsules: This is supported by electron micrographs demonstrating 200 Å rod shaped forms unraveling from around the central core of Dane particles after treatment with detergents.

The National Research Council has suggested the following nomenclature for the antigens and antibodies associated with Hepatitis B infection.⁶

HB _s Ag	The hepatitis B antigen found on the surface of the "Dane particle"
--------------------	---

and on the unattached 200 Å particles. This is synonymous with the Australia Antigen described by Blumberg.

HB _c Ag	The hepatitis B antigen found within the core of the "Dane particle."
anti-HB _s	Antibody to the hepatitis B surface antigen
anti-HB _c	Antibody to the hepatitis B core antigen

The duality of the hepatitis B antigen-antibody system has only recently been appreciated. Preliminary studies suggest that assays for anti-HB_c may be of value as screening tests for blood contaminated with the Hepatitis B virus.⁵ Additional investigation of HB_cAg and its antibody are needed to determine whether tests for their detection will be useful clinical or epidemiologic tools.

Although HB_sAg (Australia Antigen) was originally described as a single antigen, it is now apparent that it is immunologically heterogeneous.⁷ At least 5 antigenic determinants (*a*, *d*, *γ*, *w*, and *r*) have been detected. Determinant *a* is common to most antigenic particles. Determinants *d* and *γ* seem to be mutually exclusive alleles as are the *w* and *r* determinants. These determinants appear to reflect the genotype of virus.

Heterogeneity of HB_sAg is of practical importance for several reasons.⁸ First, optimal blood bank screening reagents must be able to detect all subtypes of HB_sAg. Secondly, the variable clinical picture seen with Hepatitis B infections may in part be related to the heterogeneity of the Hepatitis B viruses. Infections associated with the *d* determinant may be more likely to produce chronic disease than infections associated with the *γ* determinant. Thirdly, the ability to subtype HB_sAg is of epidemiologic value. In one study, all patients and personnel of a hemodialysis unit who developed hepatitis B, had the same subtype.⁹ In contrast both subtypes occurred equally in other hospitalized patients. This suggested a single source of infection within the dialysis unit. Lastly, heterogeneity of HB_sAg may be of consequence in the development of vaccines. Separate vaccines may be required for each viral subtype.

The ability to detect an antigen associated with the Hepatitis B Virus has permitted the immunologic differentiation of Hepatitis B from other types of viral hepatitis. For over three decades the term "infectious hepatitis" has been used interchangeably with Hepatitis A while the term "serum hepatitis" has been synonymous with Hepatitis B. This association

of terms which connote particular routes of exposure to specific viral strains has proved confusing. Epidemiologic data derived with the help of HB_sAg testing indicate that both Virus A and B can result in the clinical syndrome of infectious hepatitis. Similarly, both virus A and B appear capable of producing post transfusional hepatitis.⁸ Three large studies demonstrate that 25 to 55% of hepatitis B is endemically derived by inapparent or nonparenteral routes.^{10,11,12} This is consistent with observations that Hepatitis B is endemic in some institutions for the retarded. Outbreaks of nonparenterally transmitted Hepatitis B have been reported in hospital settings and in personnel of hemodialysis units. There is good circumstantial evidence for the sexual transmission of Hepatitis B, and Hepatitis B has been implicated in at least one epidemic of infectious hepatitis.⁸

Serologic evidence of hepatitis B infection is often absent in patients with post transfusion hepatitis. These cases are presumably a result of infection with other agents including virus A. The introduction of HB_sAg screening procedures into blood banks has reduced the incidence of post transfusion hepatitis by about a third and is likely to further reduce the percentage of post transfusion hepatitis caused by virus B.⁸ In the light of these current epidemiologic data, use of the terms "infectious" and "serum" hepatitis no longer seems appropriate.

References

1. BLUMBERG, B. S., GERSTLEY, B. J. S., HUNGERFORD, D. A., LONDON, W. T., SUTNICK, A. I.: A serum antigen (Australia antigen) in Down's syndrome, leukemia and hepatitis. *Ann. Intern. Med.*, 1967, 66:924.
2. DUDLEY, F. J., FOX, R. A., SHERLOCK, S.: Cellular immunity and hepatitis associated, Australia antigen liver disease. *Lancet*, 1972, 1:723.
3. KIM, C. Y., TILLES, J. G.: Purification and biophysical characterization of hepatitis B antigen. *J. Clin. Invest.*, 1973, 52:1176.
4. DANE, D. S., CAMERON, C. H., BRIGGS, M.: Virus-like particles in serum of patients with Australia antigen-associated hepatitis. *Lancet*, 1970, 1:695.
5. HOOFNAGLE, J. H., GERETY, R. J., NI, L. Y., BARKER, L. F.: Antibody to Hepatitis B Core Antigen. *New Eng. J. Med.*, 1974, 290:1336.
6. Center for Disease Control. Nomenclature of antigens associated with viral hepatitis, type B. *Morbidity and Mortality Weekly Report*, 1974, Vol. 23, No. 4, 1974.
7. BANCROFT, W. H., MUNDON, F. K., RUSSELL, P. K.: Detection of additional antigenic determinants of hepatitis B antigen. *J. Immunol.*, 1972, 109:842.
8. GINSBERG, A. L.: "Viral Hepatitis", in Tice: *Practice of Medicine*, Harper & Row Publishers, 1974, Vol. 7, Chap. 35.
9. MOSLEY, J. W., EDWARDS, V. M., MEIHAUS, J. E., GORDON, I., REDEKER, A. G.: Hepatitis B antigen subtyping of hemodialysis-associated infections. *Gastroent.*, 1972, 62:180.
10. GINSBERG, A. L., CONRAD, M. E., BANCROFT, W. H., LING, C. M., OVERBY, L. R.: Prevention of endemic HAA positive hepatitis with gamma globulin: Use of a simple radioimmune assay to detect HAA. *New Eng. J. Med.*, 1972, 286:562.
11. PRINCE, A. M., HARGROVE, R. L., SZMUNESS, W., CHERUBIN, C. E., FONTANA, V. J., JEFFRIES, G. H.: Immunologic distinction between infectious and serum hepatitis. *New Eng. J. Med.*, 1970, 282:987.
12. LEWIS, J. H., BRANDON, J. M., GORENC, T. J., MAXWELL, N. G.: Hepatitis B: A study of 200 cases positive for hepatitis B antigen. *Am. J. Dig. Dis.*, 1973, 18:921.

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SCIENTIFIC ARTICLES

Benign Recurrent Cholestasis: A Manifestation of Pancreatitis

FERNANDO A. SALAZAR, M.D., BERNARD A. HECKMAN, M.D., WILLIAM O. DOBBINS, III, M.D. AND STUART H. DANOVITCH, M.D.

Abstract

A 50 year old black woman was followed for three years with a recurrent cholestatic syndrome thought to be typical of benign recurrent intrahepatic cholestasis. Evidence for pancreatitis was detected during her most recent attack of jaundice.

Observations of hepatic clearance of BSP from plasma, BSP transport maximum and storage capacity, as well as light and electron microscopy, are consistent both with previous observations made in patients with benign recurrent intrahepatic cholestasis and in patients with extrahepatic biliary tract obstruction. A careful review of the literature suggests that pancreatitis may be responsible for some of the cases formerly referred to as benign recurrent intrahepatic cholestasis.

Introduction

In 1959, Summerskill and Walshe described a syndrome of benign, recurrent, intrahepatic "obstructive jaundice"¹, later characterized by recurrent episodes of jaundice with severe pruritis and the biochemical characteristics of cholestasis, bile plugs in liver biopsy specimens, normal intra- and extrahepatic bile ducts visualized at laparotomy by direct cholangiography, absence of factors associated with intrahepatic cholestasis such as certain

We report herein a patient whom we have followed for three years. Recurrent cholestasis was documented by biochemical observations as well as by liver biopsies. Evidence of pancreatitis was documented indicating that this syndrome of benign recurrent cholestasis may be related to pancreatitis.

drugs and/or pregnancy, and symptom-free intervals of several months or years². Following the initial observation, other investigators reported similar cases³⁻¹⁸ and suggested several possible causes of the syndrome, including a) a constitutional or familial type of jaundice^{3,5,11,13}, b) aberrant cholestatic hepatitis⁴, c) recurrent hepatitis of environmental origin⁹, d) endogenous progestational hormones^{15,17}, and e) more recently pancreatitis². Whereas a familial relationship has been suggested^{11,13}, most authors emphasize the lack of a familial history of jaundice in these patients^{1,6,8-10,16}. The syndrome occurs worldwide, with cases reported from America, Asia, Australia and Europe.

We report herein a patient whom we have followed for three years who appeared to suffer from this syn-

drome. Recurrent cholestasis was documented by biochemical observations as well as by liver biopsies. Other causes of intra- and extrahepatic cholestasis were carefully sought for and excluded until her most recent episode of jaundice in June 1970. At this time evidence of pancreatitis was documented indicating that this syndrome of benign recurrent cholestasis may be related to pancreatitis as suggested by Tygstrup and Jensen².

Case Report

A fifty year old black woman (P. R.) was referred to the Gastroenterology Clinic of the Washington Hospital Center in March 1969 with the diagnosis of alcoholic cirrhosis. The history revealed at least two previous prolonged episodes of jaundice associated with dark urine, generalized itching, malaise, weight loss and upper abdominal pain, at ages 18 (1939) and 44 (1964), as well as several brief attacks of jaundice and itching in the intervening years. In 1968, hepatomegaly and hyperphosphatasemia (Table 1.) were detected following a visit to our Surgical Clinic. Jaundice and itching recurred in the absence of pain in January 1969. The patient was instructed to stop her daily alcoholic consumption (one-half pint whiskey) of 25 years duration. During the Spring of 1969, her symptoms and

PANCREATITIS PRODUCING BENIGN RECURRENT CHOLESTASIS

SALAZAR, HECKMAN, DOBBINS AND DANOVITCH

TABLE 1. LABORATORY AND RADIOGRAPHIC DATA

	SGOT	SGPT	Alk.P'tase	Amylase	Lipase	Bilirubin (T/D)	Cholesterol	Carotene	BSP	Prox.*	Oral Cholecystogram	IV Cholangiogram	Liver Scan (Au ¹⁹⁸)
	Normal	<40	<40	<2.3	(70-200u)	<1.0	150-250	50-300	<5	P/C			
Date	SFU†	SFU	BLU‡	Somogyi U	IU	mg/100 ml	mg/100 ml	µg/100 ml	%	sec			
3/68	-	-	13.6	-	-	1.0/0.4	-	-	8.5	16.1/14.0	Normal	-	-
4/68	-	-	7.0	-	-	0.3/0.1	-	-	-	13.2/13.9	-	-	-
1/69	87	-	-	-	-	7.2/4.1	-	-	-	-	-	-	-
3/69	-	-	-	-	-	1.7/0.6	-	-	-	12.6/13.8	-	-	-
4/69	25	-	3.4	-	-	-	-	-	-	-	Faint visualiz.	-	-
7/69	140	60	8.0	-	-	8.4/5.2	194	-	-	-	-	-	-
8/69	25	19	5.3	122	0.5	8.0/4.5	193	25	-	11.7/13.8	-	-	Diffuse enlargement no splenic uptake
9/69	6	16	3.9	-	-	0.5/0.1	200	-	-	-	Normal	-	-
10/69	-	-	2.8	-	-	0.4/0.1	-	-	-	-	-	Normal	-
3/70	15	15	2.7	157	0.8	0.3/0.2	221	54	1.0	14.7/13.8	-	-	Normal
6/70	201	139	9.0	316	2.2	2.0/1.1	218	-	-	-	-	Abnormal	-
7/70	13	17	3.7	92	1.4	0.4/0.1	-	36	-	-	-	-	-

* Prothrombin time (Patient/control)

† Sigma-Frankel Units

‡ Bessey-Lowrey Units

liver function improved, but with recurrence in July 1969 the patient was hospitalized.

At that time symptoms included jaundice, generalized pruritis, dark urine, weakness, nausea and a twenty pound weight loss. She stated that she had resumed consumption of alcohol. There was no history of recent or past drug ingestion. Her menstrual periods were normal. Past medical history was unremarkable. The patient had never been pregnant. Her mother (age 66) had had an episode of jaundice lasting three weeks, unassociated with pruritis, approximately 20 years earlier, with complete recovery. Physical examination of the patient's mother in 1969 was entirely within normal limits. Our patient has no siblings, and no other family history of jaundice could be elicited.

Physical examination in August 1969 showed an anxious woman, continually scratching herself, with multiple excoriations of her skin. No stigmata of chronic liver disease were

present. The sclerae were icteric and her liver was palpable 10 cm below the right costal margin. Laboratory abnormalities at that time are detailed in Table 1. A percutaneous liver biopsy was performed and will be discussed. A diagnosis of benign, recurrent, intrahepatic cholestasis was considered, and the patient was discharged on cholestyramine, 12 g daily, and multivitamins. One month after discharge, she was asymptomatic, her liver smaller, and cholestyramine was discontinued. Subsequent cholecystography and intravenous cholangiography were normal. An oral glucose tolerance test was characteristically diabetic with a two hour blood sugar concentration of 140 mg/100 ml (true glucose).

The patient was re-admitted to the Metabolic Research Unit of the Washington Hospital Center in March 1970 for further study and a secretin test was performed. On admission she was completely asymptomatic and had gained 34 pounds. She was no longer consuming alcohol. Physical examina-

tion showed no scleral icterus; the patient was not scratching and her liver span was 10 cm at the midclavicular line. Liver function studies were normal (Table 1.). A repeat percutaneous liver biopsy was obtained for both light and electron microscopic studies. Following completion of these and other studies the patient was discharged and remained asymptomatic until June 1970 when painless jaundice and pruritis recurred in association with resumption of drinking. Intravenous cholangiography at this time demonstrated choledochal dilatation (Fig. 1.) and was the first evidence implicating extrahepatic biliary tract obstruction as a cause of recurrent attacks of pruritis and jaundice. Hypotonic duodenography at this time was unremarkable. All symptoms remitted rapidly with cholestyramine treatment (12 g daily). Subsequently the patient reentered the hospital, in 1971, for an additional attack of pancreatitis with choledochal obstruction. This proved to be due to an

inflammatory mass at the head of the pancreas noted surgically after failure of the process to resolve. After construction of a choledocho-duodenostomy, the patient rapidly improved and has been asymptomatic ever since.

Material and Methods

Routine laboratory investigations and liver function tests were performed in the Central Laboratory of the Washington Hospital Center. The disappearance of an intravenously administered dose (5 mg/Kg) of bromsulphalein (BSP) was performed in a similar fashion to Summerskill (10). During the March 1970 admission, BSP transport maximum (T_m) and storage capacity (S) were determined according to the method of Wheeler *et al*¹⁹. Liver biopsy specimens were obtained with a Menghini needle, and a portion was fixed in 10% formalin and stained for light microscopical study with hematoxylin and eosin as well as with stains to detect iron, bilirubin, and lipofuscin. A portion was also promptly fixed in osmium tetroxide and embedded in Epon for electron microscopical study.

Following fluoroscopic placement of a double-lumen Dreiling tube and collection of a control specimen of duodenal contents, one unit per Kg of body weight of Boots secretin was injected intravenously and three 20 minute samples of duodenal contents were aspirated, the volume measured and bicarbonate content quantitated. Following completion of the secretin test, 25 ml of a 50% $MgSO_4$ solution were infused into the gastric tube and duodenal contents were aspirated for microscopic study to detect the presence of abnormal crystals. The specimens obtained following secretin stimulation were also scrutinized for cholesterol and bile pigment crystals.



FIG. 1. Intravenous cholangiogram performed in June 1970 demonstrating choledochal dilatation (2.4 cm) and absence of contrast medium in the duodenum. No obvious cause for the obstruction is apparent. A repeat study 3 weeks later demonstrated persistent, though less (1.7 cm), choledochal dilatation. No subsequent studies have been performed.

PANCREATITIS PRODUCING BENIGN RECURRENT CHOLESTASIS

SALAZAR, HECKMAN, DOBBINS AND DANOVITCH

Results

Routine Tests of Liver Function. As outlined in Table 1., elevated serum alkaline phosphatase activity and BSP retention, as well as minimal prolongation of the prothrombin time, were noted in March 1968. An oral cholecystogram done at that time was normal. In January 1969 the patient became jaundiced, with the total serum bilirubin concentration reaching 7.2 mg/100 ml. At that time serum aspartic-aminotransferase activity (SGOT) was 87 Sigma-Frankel units (SFU). Two months later, serum bilirubin concentration had declined to 1.7 mg/100 ml, and one month thereafter serum alkaline phosphatase activity was 3.4 Bessey-Lowry units (BLU). In April 1969, oral cholecystography was repeated, and although only faintly visualized, the gall bladder appeared to contain no stones. Another episode of jaundice in the summer of 1969 was associated with a peak serum bilirubin concentration of 8.4 mg/100 ml and alkaline phosphatase activity of 8.0 BLU. At that time both the SGOT and SGPT (alanine-amino-transferase) activities were elevated and serum cholesterol concentration was within normal limits. Liver scan showed diffuse hepatic enlargement with good concentration of the isotope and no splenic or bone marrow uptake. One month later, coincidental with cholestyramine therapy, serum bilirubin concentration was normal. A third episode of hyperbilirubinemia and concomitant hyperphosphatemia, hyperamylasemia and hyperlipasemia occurred in June 1970. Cholestyramine therapy was reinstituted and during the next several weeks these abnormalities returned to normal (Table 1.). Serum protein electrophoresis had been normal on several occasions.

Studies of Duodenal Fluid and Pancreatic Function. There was a

normal volume output of 2.2 ml/Kg in response to secretin stimulation. A peak bicarbonate concentration of 48 mEq/L occurred in the 20 to 40 minute post-stimulation collection. None of these specimens contained cholesterol crystals. Gallbladder contraction was successfully stimulated with magnesium sulfate, but the contents yielded no detectable crystals. Serum amylase and lipase activities and 24 hour urinary amylase activity were within normal limits until her most recent attack of jaundice, when increased serum amylase and lipase activities were detected. Daily fecal fat excretion, while on a 100 gm fat diet, was quantitated at 6.7 gm following a 72 hour collection with a coefficient of fat absorption of 93.3%. Serum carotene concentration was 54 μ g/100 ml.

Studies of BSP Metabolism. Clearance of an intravenously administered 5 mg/Kg dose of BSP was quite rapid and the peak concentration detected at 20 minutes was only 0.41 mg/100

ml. The BSP transfer maximum was 8.2 mg/minute and the BSP storage capacity was 66.6 mg/mg/100 ml.

Liver Histology. The first percutaneous liver biopsy obtained during an attack of jaundice in August 1969 (Fig. 2.) showed severe centrilobular cholestasis by light microscopy. There were no other abnormalities noted; specifically no fatty metamorphosis, fibrosis, or Mallory bodies. A repeat percutaneous liver biopsy performed in March 1970 still showed residual centrilobular cholestasis at a time when the patient was asymptomatic and her serum bilirubin concentration was normal (Fig. 3.). This residual pigment stained positively for bilirubin with Fouchet's reagent but negatively with stains for iron and lipofuscin.

Electron photomicrographs of each liver biopsy specimen demonstrated basically normal hepatocellular structure (Fig. 4.). However, bile canaliculi were dilated and some increase in collagen content of the space of Disse was noted. Bile-like material (20, 21)

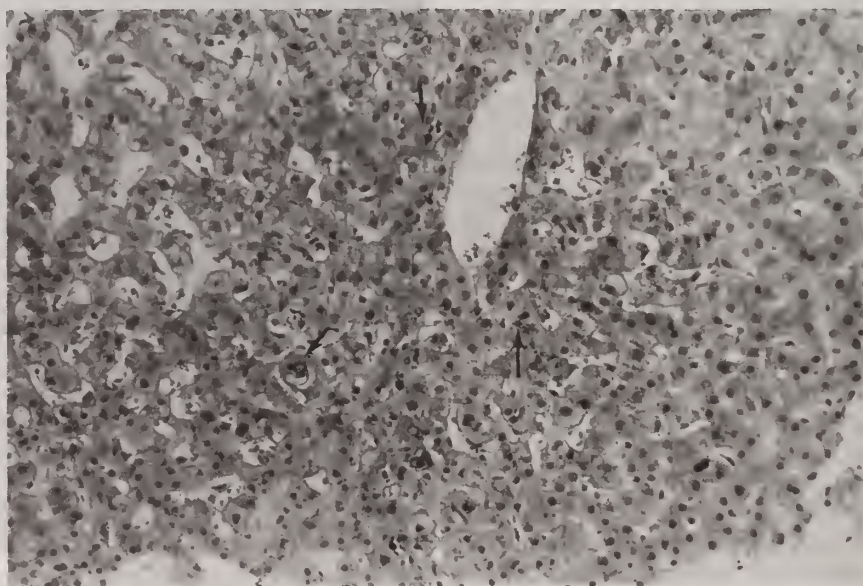


FIG. 2. Low power magnification of liver biopsy obtained when serum bilirubin concentration was 8.0 mg/100 ml. The several arrows point to areas of cholestasis which do not contrast well in black and white prints. Hematoxylin and eosin, $\times$ 50.

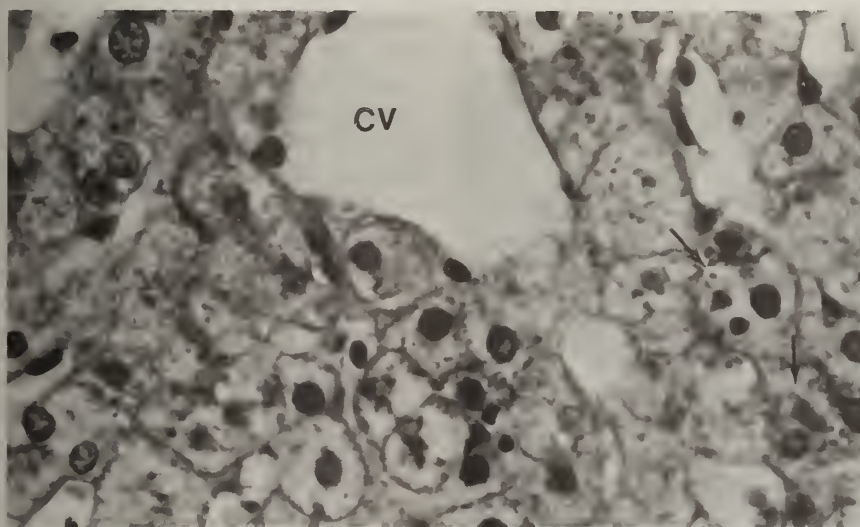


FIG. 3. Liver biopsy obtained in March 1970 when patient was asymptomatic and had a normal serum bilirubin concentration. The arrows point to residual bile pigment in the centrolobular area. Hematoxylin and eosin, $\times 200$.

was not observed within the canalicular lumens, but was noted frequently within lysosomes (heterogeneous dense bodies) of both biopsies (Fig. 4.). Occasional lipid droplets were seen within hepatocytes of both biopsies. These lipid bodies were normal in number and were similar to the "vesicles" noted in earlier studies¹⁰⁻¹².

Discussion

Prior to her most recent episode of jaundice and pruritis, our patient appeared to fulfill the criteria commonly accepted for diagnosis of benign recurrent intrahepatic cholestasis. She had had recurrent episodes of jaundice associated with severe pruritis accompanied by the biochemical abnormalities characteristic of cholestasis. Typical bile plugging was present in biopsy specimens. Her symptoms had been recurrent for 32 years, which demonstrated both the benignity of her condition as well as the recurrent nature of her ailment. Finally, three normal oral cholecystograms, coupled with a normal intravenous cholangio-

gram and inability to demonstrate biliary tract crystals in duodenal aspirates following stimulation, made it unlikely that there was significant extrahepatic biliary tract disease responsible for her recurrent cholestatic jaundice.

The possibility that recurrent pancreatitis might be responsible for her symptoms was suggested by her abnormal response to intravenous secretin stimulation in March 1970. The normal volume output coupled with the low peak bicarbonate concentration is quite characteristic of chronic pancreatitis²². Furthermore, in the presence of a negative family history of diabetes, her glucose intolerance was also suggestive of pancreatitis²³. Pancreatitis was finally confirmed during her most recent attack of jaundice (June 1970), when elevation of serum amylase and lipase activities were found along with choledochal dilatation. The occurrence of jaundice in 25% of patients with acute pancreatitis has been attributed to edema at the head of the pancreas with subsequent choledochal obstruction²⁴. In relating our

patient's recurrent attacks of pancreatitis to her alcohol intake it should be re-emphasized that no hepatotoxic effect of alcohol were noted in any liver biopsy specimen.

Do these observations, indicative of pancreatitis, preclude consideration of the diagnosis of benign recurrent cholestasis? We think not. Our patient's several attacks of jaundice and pruritis were rather atypical for that attributable to pancreatitis as they were often very prolonged, lasting several weeks, and unassociated with other features characteristic of pancreatitis. Furthermore, a review of the 29 reported cases of benign recurrent intrahepatic cholestasis (Table 2.) reveals the following information. Four patients had unequivocal evidence of pancreatitis co-existing with a recurrent cholestatic syndrome, which led the investigators reporting these cases to consider this syndrome to be a manifestation of pancreatitis². Of the remaining case reports only two specifically mentioned a normal pancreas ascertained at the time of laparotomy^{8,13}. Detailed assessment of pancreatic function and a description of the pancreas at surgery are lacking in the remaining cases, and in fact, four patients were not operated upon. In addition, pregnancy occurred during one attack of jaundice in at least three patients^{1,15,17} and a possible drug induced jaundice occurred in two others^{13,14}, one of whom also had a radio-opaque stone noted on a plane film of his abdomen and who subsequently underwent cholecystectomy. Still another patient¹⁰ had gall stones in association with her cholestatic syndrome. It would appear that pancreatitis has not been adequately excluded in a majority of the cases reported, and other causes of cholestasis such as pregnancy, drugs and cholelithiasis occasionally may be implicated. Our experience attests to the difficulty in detecting pancreatitis.

PANCREATITIS PRODUCING BENIGN RECURRENT CHOLESTASIS

SALAZAR, HECKMAN, DOBBINS AND DANOVIATCH

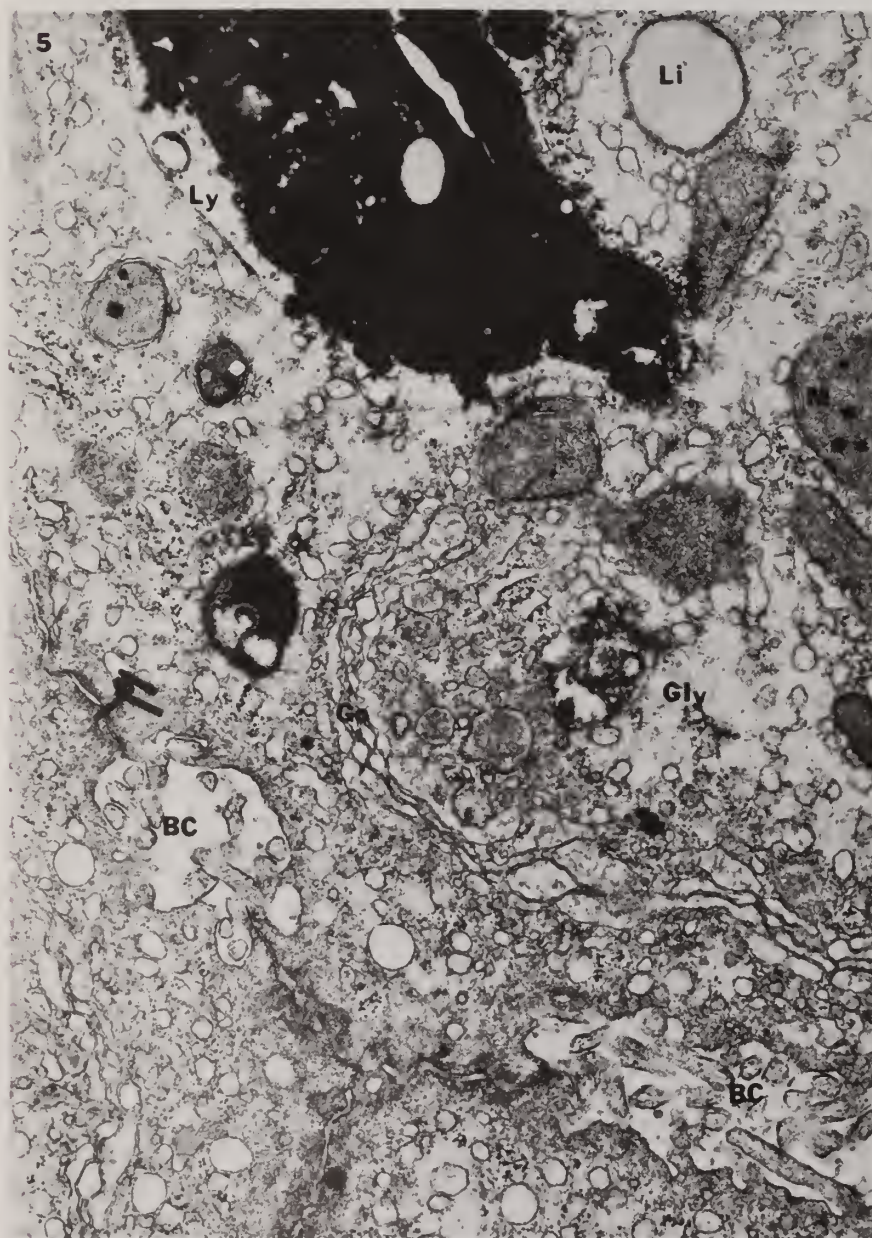


FIG. 4. Electron micrograph of portions of four hepatocytes from the second liver biopsy showing a slightly dilated bile canaliculus (BC) and numerous heterogeneous dense bodies or lysosomes (L). The smooth endoplasmic reticulum (SER) is prominent and the surrounding glycogen did not stain in this preparation. The mitochondria and other organelles appear to be normal. $\times 12,500$.

However, we do not wish to imply that all cases reported as benign recurrent intrahepatic cholestasis were solely a manifestation of pancreatitis, but feel pancreatic disease should be excluded in all patients suspected of suffering from benign recurrent intrahepatic cholestasis.

Our studies of BSP uptake by the liver are similar to observations by Williams *et al*⁹ and Summerskill¹⁰ who demonstrated normal hepatic clearance of BSP from the circulation of patients with benign recurrent intrahepatic cholestasis. During the icteric phase of this syndrome BSP transfer maximum and storage capacity have been shown to be reduced, but to return to normal when the icterus remits¹⁴. These observations are consistent with either intra- or extrahepatic obstruction to bile flow²⁵. Tygstrup has found a reduction in BSP Tm in the quiescent phase of this illness although the relative storage capacity was normal in three of four patients². The normal Tm and S measured in our patient when she was asymptomatic is more consistent with the data of Biempica *et al*¹⁴, and implies no persistent defect in hepatic metabolism of this anion.

The light microscopic appearance of liver specimens from our patient is typical for benign recurrent intrahepatic cholestasis¹⁻¹⁷ but is also consistent with extrahepatic obstruction²⁶. One interesting observation is the presence of centrolobular bile pigment in the second liver biopsy at a time when the patient was asymptomatic and had a normal serum bilirubin concentration. The special stains utilized confirmed that the pigment was in fact bilirubin. Electron microscopical observations suggested that the bile pigment was contained within lysosomes. Perhaps prolonged recurrent cholestasis resulted in the accumulation of bile pigment within the liver cell, necessitating other than

Table 2. Details of Previously Reported Cases of Benign Recurrent Intrahepatic Cholestasis.*

TABLE 2. RESULTS OF FUNCTIONAL TESTS OF PANCREAS																			
Reference	Case#	Age	Sex	History		Alcohol	Radiography		Tests of Pancreatic Function					Surgery			Liver Histology		
				Pregnancy	Drugs		Oral CB	IVC†	Serum Amylase	Lipase	Urinary Amylase	Calcification by x-ray	Duodenal Drainage	Biliary Tract	Operative Cholangiogram	Description of Pancreas	Operative Procedure	LM**	EM‡
1.	Case 1	29	F	4th month	None	Seldom	-	Normal	-	-	-	-	-	Normal	Normal	-	Exploration	Cholestasis	No
	Case 2	33	M	-	None	Seldom	Normal	Normal	-	-	-	-	-	Normal	Normal	-	T-tube drainage	Cholestasis	No
2.	Case 1	12	M	-	-	None	Normal	-	-	-	-	-	-	Normal	-	Firm	Cholecystectomy	Cholestasis	No
		15	M	-	-	-	-	-	-	-	†	-	-	Normal	Normal	Normal	Exploration	-	-
	Case 2	7	M	-	-	None	Normal	-	-	-	Normal	-	-	Normal	None	-	Exploration	Cholestasis	No
	Case 3	22	M	-	-	None	Normal	-	-	-	†	-	-	Normal	None	-	Exploration	Cholestasis	No
	Case 4	19	M	-	-	None	Normal	-	-	-	†	Yes	-	Normal	Normal	Normal	Exploration	Cholestasis	No
	Case 5	21	M	-	-	None	-	-	-	-	†	-	-	Abnormal	Normal	Firm	Choledochotomy	Cholestasis	No
		23	-	-	-	-	-	-	-	-	†	-	-	8 stones	-	-	-	-	-
		24	-	-	-	-	-	-	-	-	-	-	-	Abnormal	Firm	-	-	-	-
3.	Case 1	Cases 1 and 2, reference 2.																	
	Case 2																		
4.	Case 1	19	M	-	-	-	Normal	Normal	-	-	-	-	Normal	No Surgery	-	-	Exploration	Cholestasis	No
	Case 2	-	-	-	-	-	-	-	-	-	-	-	-	Normal	Normal	-	Exploration	Cholestasis	No
5.	Case 1	18	F	-	-	-	-	-	-	-	-	-	-	Normal	Normal	-	Exploration	Cholestasis	No
	Case 2	17	F	-	-	-	-	-	-	-	-	-	-	Normal	-	-	Cholecystectomy	Cholestasis	No
6.	Case 1	19	F	-	None	-	-	-	-	-	-	-	-	Normal	-	-	Exploration	Cholestasis	No
		31	F	-	None	Rare	Normal	-	-	-	-	-	Normal	Normal	Normal	-	Exploration	Cholestasis	No
7.	Case 1	14	F	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Yes
8.	Case 1	9	F	-	-	-	-	-	-	-	-	-	-	Normal	Normal	Normal	Exploration	Cholestasis	No
		11	-	-	-	-	Normal	-	-	-	-	-	-	Normal	-	-	T-tube drainage	Cholestasis	-
9.	Case 1	34	F	-	-	-	-	-	-	-	-	-	-	Normal	Normal	-	Exploration	Cholestasis	No
	Case 2	24	F	-	-	-	-	-	-	-	-	-	-	Normal	Normal	-	Exploration	Cholestasis	No
	Case 3	31	F	-	-	-	-	-	-	-	-	-	-	Normal	Normal	-	Exploration	Cholestasis	No
	Case 4	37	F	-	Same as Case 2, Reference 1.	-	-	-	-	-	-	-	-	Normal	Normal	-	Exploration	Cholestasis	No
10.	Case 1	54	F	-	-	-	GB Stones	-	Normal	-	-	-	-	CB Stone	-	-	Cholecystectomy	Cholestasis	Yes
		57	-	-	-	-	-	Normal	-	-	-	-	-	-	Normal	-	T-tube drainage	Cholestasis	-
11.	Case 1	24	F	-	-	-	-	-	-	-	-	-	-	Normal	Normal	-	Cholecystectomy	Cholestasis	Yes
	Case 2	18	F	-	-	-	-	-	-	-	-	-	-	Normal	Normal	-	T-tube drainage	Cholestasis	Yes
12.	Case 1	Case 1, Reference 10																	
	Case 2	Case 2, Reference 1																	
13.	Case 1	-	M	-	-	-	-	-	-	-	-	-	-	Normal	-	Normal	Exploration	Cholestasis	No
		-	-	-	Anti-depressants	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	Case 2	-	M	-	-	-	-	-	-	-	-	-	-	No Surgery	-	-	-	-	No
14.	Case 3	20	M	-	-	-	-	-	-	-	-	-	-	Normal	Normal	-	Exploration	-	-
	Case 1	27	M	-	Tolbutamide	-	Radiopaque stones	-	-	-	-	-	-	-	Normal	-	Cholecystectomy	Cholestasis	Yes
15.	Case 1	19	F	-	-	-	-	-	-	-	-	-	-	RUQ Adhesions	Normal	-	Exploration	Cholestasis	No
		27	-	9th month	-	-	-	-	-	-	-	-	-	Normal	None	-	Exploration	-	-
	Case 1	8	F	-	-	-	-	-	-	-	-	-	-	Normal	Normal	-	Exploration	Cholestasis	No
17.	Case 1	28	F	Yes	-	-	-	-	-	-	-	-	-	Surgery Not Commented On	-	-	-	-	Yes
18.	Case 1	24	F	-	None	-	-	-	-	-	-	-	-	Normal	Normal	-	Exploration	Cholestasis	No
Present Case		49	F	None	None	Yes	Normal	Normal	Normal	Normal	Normal	None	Abnormal	No Surgery	-	-	-	Cholestasis	Yes
		50	None	None	None	Yes	Normal	Abnormal	†	†	Not done	None	Not done	-	-	-	-	Cholestasis	Yes

* Entries in this table indicate known information. The dash marks (-) indicate that the observation in question was not commented upon in the case reports.

† IVC, Intravenous cholangiogram

†† LM, Light microscopy

‡ EM, Electron microscopy; a "No" indicates the procedure not done.

††† †, Increased

PANCREATITIS PRODUCING BENIGN RECURRENT CHOLESTASIS

SALAZAR, HECKMAN, DOBBINS AND DANOVITCH

usual means for disposal of this bile pigment—hence, uptake and digestion by lysosomes. Among the acid hydrolase activities known to reside within lysosomes is that of beta-glucuronidase^{2,7}. This activity may catalyze the deconjugation of bilirubin diglucuronide to unconjugated bilirubin which is insoluble, and perhaps incapable of further intracellular transport or metabolism, thus accounting for the persistence of pigment in the second liver biopsy specimen. Maki has shown that bilirubin diglucuronide can be a substrate for lysosomal beta-glucuronidase activity derived from certain strains of *E. coli* which, if present in gall bladder bile, generate insoluble bile pigment stones^{2,8}.

Including this report, there are six electron microscopic studies of liver biopsies obtained from patients with the clinical syndrome of benign recurrent intrahepatic cholestasis^{7,10-12,14}. Three reports noted "vesicles" within hepatocytes thought to be characteristic of this syndrome¹⁰⁻¹². Two reports^{7,14} and our study fail to confirm this. Rather, the vesicles probably represent normally present lipid bodies¹⁴. Biempica *et al* observed minor variations in fine structure of hepatocytes from a biopsy specimen taken from their patient during an exacerbation, whereas during clinical remission they noted small amounts of intracellular and intracanalicular bile pigment, some glycogen-rich nuclei, and the presence of crystalloid nucleoids within microbodies¹⁴. We detected small amounts of intracellular bile pigment in the biopsy specimen obtained during remission but note no other changes. Da Silva and de Brito found microvilli of bile canaliculi to be "edematous" and reduced in number¹¹ whereas, Schubert *et al* noted the presence of numerous lysosomes and increased numbers of large mitochondria with "peculiar" configurations⁷. However,

none of the electron microscopic changes noted in these six reports can be considered specific for this syndrome and are commonly seen in a wide variety of hepatic disorders including extrahepatic obstruction^{21,29}.

Therapeutic recommendations for patients with this disorder include biliary drainage with a T-tube inserted into the choledochus^{6,11}, corticosteroids^{5,9} and cholestyramine^{7,8}. Concomitant with cholestyramine therapy at a daily dose of 12 gm, pruritis promptly remitted and serum bilirubin concentration declined on both occasions when treatment was begun in our patient. It is likely that she would have recovered spontaneously and that the response witnessed was coincidental with remission of the choledochal obstruction.

References

- SUMMERSKILL, W. H. J., WALSHE, J. M.: Benign Recurrent Intrahepatic Obstructive Jaundice, *Lancet*, 2:686-690, 1959.
- TYGSTRUP, N., JENSEN, B.: Intermittent Intrahepatic Cholestasis of Unknown Etiology in Five Young Males from the Faroe Islands, *Acta Med. Scand.*, 185:523-530, 1969.
- TYGSTRUP, N.: Intermittent Possibly Familial Intrahepatic Cholestasis, *Lancet*, 1:1171-1172, 1960.
- de GROTE, J., GOUBEAU, P., VANDENBROUCKE J.: Ictere Cholestatique Recidivant, *Acta Gastroent Belg.*, 23:747-755, 1960.
- KUHN, H. A.: Intrahepatic Cholestasis in Two Brothers, *German Med. Monthly*, 8:185-188, 1963.
- SCHAPIRO, R., ISSELBACHER, K. J.: Benign Recurrent Intrahepatic Cholestasis, *New Eng. J. Med.*, 268:708-711, 1963.
- SCHUBERT, W. K., GARANCIS, J., PERRIN, E.: Idiopathic Benign Recurrent Cholestasis (Abstract), *Clin. Res.*, 13:409-409, 1965.
- SPIEGEL, E. L., SCHUBERT, W., PERRIN, E., SCHIFF, L.: Benign Recurrent Intrahepatic Cholestasis with Response to Cholestyramine, *Am. J. Med.*, 39:682-688, 1965.
- WILLIAMS, R., CARTER, M. A., SHERLOCK, S., SCHEUER, P. J., HILL, K. R.: Idiopathic Recurrent Cholestasis. A Study of the Functional and Pathological Lesions in Four Cases, *Quart. J. Med.*, 33:387-399, 1964.
- SUMMERSKILL, W. H. J.: The Syndrome of Benign Recurrent Cholestasis, *Am. J. Med.*, 38:298-305, 1965.
- da SILVA, L. C., de BRITO, T.: Benign Recurrent Intrahepatic Cholestasis in Two Brothers, A Clinical, Light and Electron Microscopy Study. *Ann. Int. Med.*, 65:330-341, 1965.
- DICKSON, E. R., FLETCHER, J., SUMMERSKILL, W. H. J.: Ultrastructural Changes of the Liver in Benign Recurrent Cholestasis, *Mayo Clin. Proc.*, 40:288-295, 1965.
- GOLDBERG, D. M., HENDRY, E. B.: Familial Form of Benign Idiopathic Recurrent Cholestasis, *Arch. Int. Med.*, 120:556-564, 1967.
- BIEMPICA, L., GUTSTEIN, S., ARIAS, I.: Morphological and Biochemical Studies of Benign Recurrent Cholestasis, *Gastroenterology* 52:521-535, 1967.
- STATHERS, G., REED, C. S. H., HURST, E.: Idiopathic Recurrent Cholestasis, *Gastroenterology*, 52:536-543, 1967.
- STARK, H.: Benign Recurrent Cholestasis in a Child, *Pediatrics*, 41:636-639, 1968.
- BERKOWITZ, D., NADKARNI, B. G.: Benign Recurrent Intrahepatic Cholestasis Associated with Pregnancy (Abstract), *Gastroenterology*, 52:1071-1071, 1967.
- ITOH, S., SETA, K.: Benign Recurrent Intrahepatic Jaundice, *Acta Hepatosplen*, 15:227-233, 1968.
- WHEELER, H. O., MELTZER, J. I., BRADLEY, S. E.: Biliary Transport and Hepatic Storage of Sulfobromophthalein Sodium in Unanesthetized Dog, in Normal Man, and in Patients with Hepatic Disease, *Journal of Clinical Investigation*, 39:1131-1144, 1960.
- BIAVA, C. G.: Studies on Cholestasis. A Re-evaluation of the Fine Structures of Normal Human Bile Cana-

- liculi, Lab. Invest., 13:840-864, 1964.
21. SASAKI, H., SCHAFFNER, F., POPPER, H.: Bile Ductules in Cholestasis: Morphologic Evidence for Secretion and Absorption in Man, Lab. Invest., 16:84-95, 1967.
 22. DREILING, D. A., JANOWITZ, H. D.: Secretion of Electrolytes by the Human Pancreas, Gastroenterology, 30:382-390, 1956.
 23. RUSH, A., BOCKUS, H. L.: Chronic Pancreatitis, Relapsing Pancreatitis, Pancreatic Lithiasis, and Calcification of the Pancreas, chap. 127, Gastroenterology, volume III (Bockus HL, ed) Philadelphia and London, W. B. Saunders, 1965.
 24. WEINSTEIN, B. R., KORN, R. J., ZIMMERMAN, H. J.: Obstructive Jaundice as a Complication of Pancreatitis, Ann. Int. Med., 58:245-258, 1963.
 25. SCHOENFIELD, L. J., FOULK, W. T., BUTT, H. R.: Studies of Sulfobromophthalein Sodium (BSP) in Man. I. In Normal Subjects and Patients with Hepatic Disease, J. Clin. Invest., 43:1409-1418, 1964.
 26. GALL, E. A., DOBROGORSKI, O.: Hepatic Alterations in Obstructive Jaundice, Amer. J. Clin. Path., 41:126-139, 1964.
 27. WEISSMANN, G.: Lysosomes, New Eng. J. Med., 273:1084-1090, 1965.
 28. MAKI, T.: Pathogenesis of Calcium Bilirubinate Gallstone: Role of E. Coli β -glucuronidase and Coagulation by Inorganic Ions, Polyelectrolytes and Agitation, Ann. Surg., 164:90-100, 1966.
 29. SCHAFFNER, F., POPPER, H.: Electron Microscopy of the Liver, Chap. 2, Diseases of the Liver (Schiff L, ed) Philadelphia and Toronto, J. B. Lippincott, 1969.

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THE VIEW BOX

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A 60 year old male is seen with progressive confusion, loss of memory and incomplete hemiparesis. In the past he experienced several Jacksonian type seizures. He is a chronic ethanol abuser. (For Diagnosis see page 581)



Hepatic Artery-Portal Vein Fistula with Hepatic Cirrhosis, Hepatoma and Bleeding Esophageal Varices

LOUIS T. KANDA, M.D., LUIS A. MISPIRETA, M.D., JOSEPH P. MOCK, M.D. AND KAREL B. ABSOLON, M.D.

Abstract

A case report of hepatic artery-portal vein fistula due to hepatoma in a cirrhotic liver is reported. Other causes of such fistulas are rupture of congenital or acquired hepatic artery aneurysm into the portal vein and penetrating abdominal trauma.

Although hepatic artery-portal vein fistula is a rare condition, it is a potentially curable cause of portal hypertension. The portal vein should be palpated for evidence of thrill before any portal systemic shunt is performed on patients with portal hypertension.

The diagnosis is suspected in a patient with a bruit on abdominal auscultation in the presence of upper gastrointestinal bleeding due to esophageal varices.

Arteriography establishes the diagnosis and the location of the fistula.

Treatment is surgical with direct repair when possible and ligation of the artery when repair is not feasible.

Introduction

A patient with bleeding esophageal varices due to portal hypertension produced by a combination of cirrhosis, hepatoma and hepatic-portal

In view of the extensive hepatoma in our patient only ligation of the artery could be accomplished. A portal systemic shunt without correction of the fistula would have been ill advised.

A-V fistula prompted this literature review and report.

Portal hypertension is usually a result of an obstruction in the portal venous outflow tract due to perivascular fibrosis in a cirrhotic liver. Other causes are post hepatic, as in the Budd-Chiari syndrome; or pre hepatic, as with portal vein thrombosis, external compression of the vein, or an arteriovenous fistula involving the hepatic artery and the veins of the portal system.¹ In the last case the portal pressure increase is secondary to an increased portal flow exceeding its capacity.

Fistulas of the portal system can occur between the splenic or mesenteric vessels, or the hepatic artery and its branches and the veins of the portal system. This rare cause of portal hypertension has a high cure rate in the absence of other pathologic change. Upon review of the literature it was found that the association of

cirrhosis, hepatoma and arteriovenous fistula due to tumor invasion has not previously been described.

Case Report

J. M., a 67-year-old black male, a known alcoholic until twenty years ago, was admitted to the Washington Hospital Center for the first time seven years ago with upper gastrointestinal hemorrhage. An upper gastrointestinal series and esophagogram showed esophageal varices. The bleeding stopped spontaneously and the patient was discharged without blood transfusion. A year later he was readmitted for the same problem and again the bleeding stopped spontaneously. He did well for about seven years when he was readmitted for the third time in shock with a massive gastrointestinal hemorrhage. Despite blood transfusions, iced saline irrigation of the stomach and tamponade with a Sengstaken-Blakemore tube, the patient bled again massively a few hours later. A transfemoral mesenteric artery picrotressin drip (2mg/hm) controlled the bleeding temporarily. Arteriography showed that the celiac axis and the superior mesenteric artery originated from a common trunk. Two hepatic arteries, a larger one arising from the

HEPATIC ARTERY-PORTAL VEIN FISTULA

KANDA, MISPIRETA, MOCK AND ABSOLON

superior mesenteric artery with two separate take offs and a smaller one from the celiac axis, were identified. (Figure 1) A large area of vascularity occupying almost the entire right lobe of the liver was suggestive of a hepatoma. This was supported by the liver scan using 4MmCl of Tc99-M-S-colloid I.V. and a positive alpha fetoglobulin. The contrast material entered the distal portal vein and the periphery. (Figures 2, 3)

An upper gastrointestinal series and endoscopy demonstrated bleeding esophageal varices in the mid and lower esophagus and showed no other abnormal change. The stomach and duodenum were normal.

Laboratory studies, with the exception of a hemoglobin of 8.8 gm% and hematocrit of 27%, were all within normal limits. An exploratory celiotomy revealed a grossly nodular and cirrhotic liver with a large irregular mass occupying its right lobe with extension into the porta hepatis. Palpation of the portal vein in this area revealed a thrill. This thrill disappeared on occlusion of the hepatic artery originating from the superior mesenteric artery. The veins around the upper gastrointestinal tract were noted to be distended. Portal vein pressures and PO_2 were 39 mm/Hg and 99 mm/Hg respectively. After ligation of this hepatic artery, these values changed only to 37 mm/Hg and 41 mm/Hg, but the thrill disappeared. Histological examination of the mass showed hepatoma. Biopsy of the left lobe showed postnecrotic cirrhosis. In view of extension of the tumor to the porta hepatis no additional procedures were performed.

The postoperative course was uneventful. Transaminase and alkaline phosphatase levels were initially elevated, but returned to normal within four days. A repeated celiac axis arteriogram eleven days postoperatively showed the hepatic artery from



FIG. 1. Common origin for the celiac axis and superior mesenteric artery. Both hepatic arteries can also be seen. Note the double take off for the inferior right hepatic artery. (at arrows)



FIG. 2. Pear shape pool of contrast material just to the right of the 11th vertebra and corresponding to the distal



FIG. 3. In the venous phase, the portal vein is noted and its superior end overlies the contrast area seen in Figure 1.

the superior mesenteric artery ligated; the abnormal filling area was again noted, but the filling was delayed. Four months postoperatively, the patient developed shortness of breath and a right pleural effusion. Thoracentesis and examination of the fluid showed malignant cells consistent with hepatoma. The further course of this patient was progressively downward from extension of the malignancy with death occurring seven months postoperatively but the patient did not rebleed.

Discussion

The first case of hepatic artery-portal vein fistula was reported in 1892 by Sachs, who described the condition in a child who died of hemorrhage from esophageal varices. Autopsy of this child revealed a hepatic artery aneurysm which ruptured into the portal vein.² It was not until 1952 that the second case was reported by Strickler, *et al*.³ It in-

volved a 44-year-old white woman, also with bleeding esophageal varices. Devascularization of the stomach was performed in an attempt to control the bleeding, but the patient died from exsanguination, and autopsy revealed a fistula between the right hepatic artery and the right portal vein of unknown etiology. The third case, reported by Madding *et al* in 1954,⁴ was the first antemortem diagnosis of a hepato-portal arteriovenous fistula. The fistula was found during an exploratory laparotomy for upper gastrointestinal hemorrhage. This patient died seven days postoperatively of recurrent bleeding, despite proximal and distal ligation of the hepatic artery.

In 1957 Wheeler and Warren⁵ reported the first successfully treated case. This was in a patient with bleeding duodenal varices. In the first operation the varices were directly sutured with resulting temporary control of bleeding; recurrence followed shortly after and at re-exploration, the portal vein pressure was measured and found to be elevated. A splenorenal shunt was performed. Postoperatively, on examination of the abdomen, a bruit was heard in the epigastrium. Translumbal aortogram demonstrated a hepatic artery aneurysm with a fistula into the portal vein. The fistula was closed, and the patient recovered uneventfully.

Since 1957 an additional 21 cases of hepatic artery-portal vein fistula have been reported for a total of 25 cases. Of these, the fistula was located extrahepatically in 11 patients (before the vessels enter the liver). (Table 1) Our case is the twelfth.

It is apparent that in our patient the fistula resulted from involvement of the vessels by hepatoma. As such, it is the first reported case. It is significant that none of the previously reported patients had hepatic cirrhosis, so that the portal hypertension and esophageal variceal bleeding in these patients

HEPATIC ARTERY-PORTAL VEIN FISTULA

KANDA, MISPIRETA, MOCK AND ABSOLON



FIG. 4. Shows the ligated right hepatic just below the left hepatic artery. (at arrow)

were solely due to the fistula. The patient under discussion had post necrotic cirrhosis, and with his past history of upper gastrointestinal hemorrhage, presence of esophageal varices known for at least six years, and failure of the portal vein pressure to drop significantly after occlusion of the feeding artery, it is our belief that the portal hypertension in this patient was primarily due to hepatic cirrhosis. With the subsequent development of the fistula the hypertension worsened, resulting in upper gastrointestinal hemorrhage.

Patients with fistulas from rupture of a hepatic artery aneurysm into portal veins presented with either

ascites or gastrointestinal hemorrhage from esophageal varices.⁶ However, although portal hypertension was present in the traumatic cases, none presented with ascites, esophageal varices or gastrointestinal hemorrhage. The outstanding signs and symptoms were vague abdominal pain and abdominal bruit on auscultation.⁷⁻⁹ Cohen and DeBakey have suggested that this is possible due to a slower flow in the traumatic A-V fistulas.⁸

Thal created an A-V fistula in the splenic vessels of dogs and followed them for 6-12 months with production of esophageal varices. He attributes this to the extensive development of extra-esophageal collaterals. However,

he was able to show that when the portal system and these collaterals were occluded, the creation of the splenic A-V fistula resulted in a dramatic increase in the number and size of the varices. This is similar to what happened in our patient to cause his third episode of GI bleeding.¹⁰

Creech reported a 44-year-old man in whom an arteriovenous fistula in the portal system was diagnosed thirty years after blunt abdominal injury.¹¹

The unique feature of hepatic artery-portal vein fistula is its tendency to produce portal hypertension and the potentially lethal consequences of ascites and variceal bleeding. In contrast to the deleterious cardiac effects observed in peripheral arteriovenous fistulas, patients with hepatic artery-portal vein fistulas show no heart failure and apparently no significant elevation of cardiac output. A dampening effect of the hepatic sinusoids develops, as suggested by Mooney. As shown experimentally in dogs, when the liver is interposed between an arteriovenous fistula in the hind limb and the heart the previously elevated cardiac output drops toward control levels.¹²

A bruit on abdominal auscultation of a patient with upper gastrointestinal bleeding due to esophageal varices should suggest the diagnosis of an arterial-portal vein fistula. Arteriography establishes the diagnosis and identifies its location.¹³

The treatment is surgical. Direct repair of the vessels involved is attempted when the fistula is located in the gastrohepatic ligament. When the fistula is in the hilum of the liver where repair of the vessels is technically difficult, ligation of the artery is performed.

In view of the extensive hepatoma in our patient only ligation of the artery could be accomplished. A portal systemic shunt without correction of the fistula would have been ill advised.

TABLE 1. Reported Cases of Extrahepatic Hepatic Artery-Portal Vein Fistulae

Author & Date	Presentation	Age Sex	Cause	Treatment	Followup	Portal Pressure
Sachs ² 1892	Gastrointestinal bleeding from esophageal varices	Child	Rupture of congenital hepatic artery aneu- rysm into portal vein	None	Died of exsangui- nation	Not measured
Strickler ³ 1952	Bleeding esophageal varices	49 F	Rupture of the (R) he- patic artery aneurysm (congenital) into the (R) portal vein	Gastric devascu- larization	Died postopera- tively of exsan- guination	Not measured
Madding, et. al. 1954 ⁴	Bleeding esophageal varices	48 M	Rupture of congenital hepatic artery aneu- rysm into portal vein	Ligation of hepa- tic artery proxi- mal and distal to the fistula	Died 7 days post- operatively of recurrent GI bleeding	Not measured
Wheeler & Warren 1957 ⁵	Bleeding duodenal varices	37 M	Rupture of an acquired hepatic artery aneu- rysm	Repair of vessels wiring of aneu- rysm	Alive and well	46 cm. H ₂ O
Grant, et. al. 1958 ⁷	Epigastric bruit 3 days postop	19 M	Gun shot wound of the abdomen	Closure of fistula through the portal vein	Alive and well	Elevated
Cohen & DeBakey 1960 ⁸	Continuous bruit in the RUQ 5 days postop	32 M	Gun shot wound of the abdomen	Division of fistula and repair of vessels	Alive and well	Elevated
Graham 1964 ^{1,4}	Gastrointestinal bleeding	61 M	Osler-Weber-Rendu syndrome	Resection of fis- tula and hepatic lobectomy	Died postopera- tively	
Creech 1965 ^{1,1}	Continuous murmur in epigastrium on routine checkup	44 M	Rupture of acquired hepatic artery aneu- rysm into portal vein. Blunt abdominal trauma at age 14	Direct repair of vessels	Alive and well	Not measured
Berner 1967 ^{1,5}	Abdominal bruit on followup examina- tion	21 M	Gun shot wound of ab- domen 4 years earlier	Direct repair of vessels	Alive and well	Not measured
Fulton 1970 ^{1,6}	Upper abdominal bruit	30 M	Gun shot wound 3 months earlier	Direct repair of vessels	Alive and well	17.5 cm. H ₂ O
VanWay 1971 ⁹	Abdominal pain ascites	61 F	Rupture or hepatic ar- tery aneurysm into (R) portal vein	Ligation of hepa- tic artery		38 cm. H ₂ O
Kanda, Mispireta & Absolon 1973	Gastrointestinal bleeding	67 M	Invasion of hepatic ar- tery and portal vein by tumor (hepatoma)	Proximal ligation of hepatic ar- tery	Died 7 months postoperatively of metastases	39 mmHg

HEPATIC ARTERY-PORTAL VEIN FISTULA

KANDA, MISPIRETA, MOCK AND ABSOLON

A systemic arteriovenous shunt resulting in increased cardiac output, heart failure, and an increased hepatic artery-portal flow would have resulted.

References

1. STONE, H. H., JORDAN, W. D.: Arteriovenous Fistulas. *Am. J. Surg.*, 109:191, 1965.
2. ADAMS, H. D.: Congenital AV and Cirroid Aneurysms. *Surg. Gynecol. Obstet.*, 92:693, 1951.
3. STRICKLER, J. H., LUPKIN, N., RICE, C.: Hepatic Portal Arteriovenous Fistula. *Surgery*, 31:583, 1952.
4. MADDING, G. F., SMITH, W. L., HERSHBERGER, L. R.: Hepatoportal Arteriovenous Fistula. *J.A.M.A.*, 156:593, 1954.
5. WHEELER, H. B., WARREN, R.: Duodenal Varices Due to Portal Hypertension from an Arteriovenous Aneurysm. *Am. Surg.*, 146:229, 1957.
6. FOSTER, J. H., SANDBLOM, P.: Portal Hypertension Secondary to an Hepatoportal Arteriovenous Fistula. *Ann. Surg.*, 154:300, 1961.
7. GRANT, R. N., GLIEDMAN, M. I., DETERLING, J.: Coexisting Traumatic Arterio-venous Fistulae Between the Aorta and Inferior Vena Cava, and Hepatic Artery and Portal Vein, Complicated by Goldblatt Kidney. *Ann. Surg.*, 148:286, 1958.
8. COHEN, A., DEBAKEY, M. E.: Successful Repair of Traumatic Arteriovenous Fistulas Between Hepatic Artery and Portal Vein and Right Renal Artery and Inferior Vena Cava. *Surgery*, 48:548, 1960.
9. VAN WAY, C. W. III, CRANE, J. M., RIDDELL, D. H., FOSTER, J. H.: Arteriovenous Fistula in the Portal Circulation. *Surgery*, 70:876, 1971.
10. From personal communication with Alan Thal, M.D.
11. CREECH, O., JR., GANTT, J., WREN, H.: Traumatic Arteriovenous Fistula at Unusual Sites. *Ann. Surg.*, 161:908, 1965.
12. MOONEY, C. S., HONAKER, A. D., GRIFFEN, W. O., JR.: Influence of the Liver on Arteriovenous Fistulas. *Arch. Surg.*, 100:154, 1970.
13. KAUDE, J., DUDGEON, D. L., TALBERT, J. L.: The Role of Selective Angiography in the Diagnosis and Treatment of Hepatoportal Arteriovenous Fistula. *Radiology*, 92:1971, 1969.
14. GRAHAM, W. P., EISEMAN, B., PRYOR, R.: Hepatic Artery Aneurysm with Portal Vein Fistula in a Patient with Familial Hereditary Telengectasia. *Ann. Surg.*, 159:362, 1964.
15. BERNER, C. F., COX, E., BUXTON, R. W.: Unusual Arteriovenous Fistulae Involving Hepatic Artery, Portal Vein, and Internal Iliac Vessels: Case reports and a review of the literature. *Am. Surg.*, 33:276, 1967.
16. FULTON, R. L., WOLFEL, D. A.: Hepatic Artery-Portal Vein Arteriovenous Fistula—Report of a Case with Notes on the Pathophysiology of this Condition. *Arch. Surg.*, 100:307, 1970.

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Primary Linitis Plastica Carcinoma of the Colon

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Abstract

A young black woman presenting with abdominal pain and complete obstruction of the colon with a lesion mimicking inflammatory bowel disease was found to have primary linitis plastica causing her symptoms.

Introduction

Primary linitis plastica carcinoma of the colon is a disease rarely diagnosed before surgery. Characteristically a long segment of colon is involved, often mimicking inflammatory disease of the bowel. Linitis plastica carcinoma of the colon may occur in conjunction with ulcerative colitis^{1,2} or in association with linitis plastica in other parts of the gastrointestinal tract, usually the stomach³. This report documents a new case and calls attention to this disease and to features which frequently cause confusion with inflammatory bowel disease, for misdiagnosis may delay appropriate treatment.

Report Of Case

The patient, B. Q. (WHC A149066), a 38 year old black woman, was first seen in August, 1967 with the complaints of abdominal and low back

All physicians caring for this woman were surprised at the final pathologic diagnosis of her colonic disease. It seems likely that the patient's symptoms, which began 15 months prior to her surgery, were related to this lesion.

pain of one week's duration. Left lower quadrant tenderness was noted on pelvic examination and was attributed to pelvic inflammatory disease. In the succeeding six months she was seen on several occasions because of lower abdominal discomfort and lower urinary tract symptoms. No change occurred in her bowel habits. Treatment was directed toward the lower urinary tract and apparent pelvic inflammatory disease. In August, 1968 her abdominal pain increased, and she noted slight rectal bleeding. The stools seemed to be of smaller caliber. Two months later the patient had several episodes of emesis of clear material, usually occurring early in the morning and without definite relation to eating. A barium enema examination (Fig. 1) performed in November, 1968, showed marked narrowing and fixation of the colon in the region of the

distal transverse colon, splenic flexure and the proximal descending colon. Multiple "pseudo-fistulae", which seemed to represent large ulcerations and pseudodiverticulae were noted. Neither barium nor air could be forced into the proximal colon. The impression of the radiologist was that of granulomatous colitis with obstruction of the transverse colon.

The patient was admitted to the hospital for evaluation of this radiographic lesion. She denied any weight loss, anorexia, constipation or diarrhea. Physical examination was unremarkable except for the suggestion of a mass in the right lower quadrant and marked tenderness over the entire lower abdomen. Rectal examination was negative, and there was no evidence of ano-rectal disease. Pelvic examination seemed to confirm the impression of a right lower quadrant mass.

On admission the hemoglobin was 11.9 g./100 ml. and hematocrit 35%. The white blood cell count was 7300/mm³ with a normal differential count. Her serology was non-reactive. Assessment of liver function failed to reveal any abnormalities. Concentrations of glucose, urea nitrogen, electrolytes, calcium and phosphorus in a fasting serum specimen were also normal. Sigmoidoscopic examination to 25 cm.

LINITIS PLASTICA OF COLON

BASHOUR, GOLDMAN, GERBER AND DANOVITCH



FIG. 1. Barium enema study shows obstruction to the flow of barium in the mid-transverse colon. Marked irregularity with pseudo-diverticula formation is noted in the distal portion of the transverse colon. In addition, a long "string sign" involving the splenic flexure, and adjacent descending colon can be visualized along with apparent ulceration of the distal descending colon.

from the anus failed to reveal any abnormalities. The stool was negative for ova and parasites. An intermediate strength PPD was negative. A repeat barium enema examination again revealed failure of the column of barium, or subsequent air, to pass an apparently obstructed area in the mid-transverse colon. Intravenous cholangiography and intravenous pyelography, as well as routine chest films and an electrocardiogram were normal. An upper gastrointestinal series was not performed because of the apparent obstruction in the transverse colon. Because of this obstruction, it was felt that resection of the lesion was indicated. The pre-operative diagnosis was granulomatous colitis.

Operative Findings. At the time of abdominal exploration, the liver, stomach, kidneys and small intestine were found to be normal. The omentum and entire colon from cecum to proximal sigmoid, was thickened, edematous and distorted, with apparent overgrowth of the serosal surface by mesenteric fat. The indurated mass of tissue seemed to involve the right fallopian tube and ovary. The lesion was felt to be compatible with inflammatory bowel disease, and resection of the entire colon, from cecum to proximal sigmoid, as well as 40 to 50 cm. of terminal ileum and the right fallopian tube and ovary was carried out. The patient had an uneventful post-operative recovery.

Pathologic Findings. Microscopically, sections of colon showed multiple foci of anaplastic carcinoma mainly infiltrating the submucosa and muscularis layers of the colon (Fig. 2A), with invasion of right fallopian tube and ovary. The characteristic signet cell was noted (Fig. 2B). Chemotherapy was begun with 5-fluorouracil.

Discussion

Primary linitis plastica carcinoma of the colon is indeed a rare lesion. Only 11 of 12,000 patients with carcinoma of the colon reported from the Mayo Clinic exhibited the characteristic pathologic features of linitis plastica but no evidence was presented that they were primary⁴. Nine cases of primary colonic involvement have been reported in detail^{1,2,5,6,7,8}. In three other cases, the lesion was localized to the rectum^{5,9}. In the majority of instances, linitis plastica of the colon is secondary to an associated lesion in the stomach^{3,8,10} or in other parts of the gastrointestinal tract^{11,12}.

All physicians caring for this woman were surprised at the final pathologic diagnosis of her colonic disease. It seems likely that the patient's symptoms, which began 15 months prior to her surgery, were related to this lesion. While this lesion appears to occur in all age groups and in both sexes, we think it is significant that five of the reported patients were under 45 years of age and that seven were women. This is at variance with the usual age of onset and sex predilection of adenocarcinoma of the colon⁴. The presenting symptoms vary from diarrhea to constipation, and in two instances frank obstruction to the retrograde flow of barium was present at the time of admission. In addition, constitutional symptoms of weight loss and those related to anemia were also prominent features in some cases.

Careful assessment of this patient's symptoms and physical findings might have led us to appraise the situation more objectively. For although our patient was young, and although granulomatous colitis is a disease of the young¹², the lack of diarrhea, a symptom seen in over 90% of patients

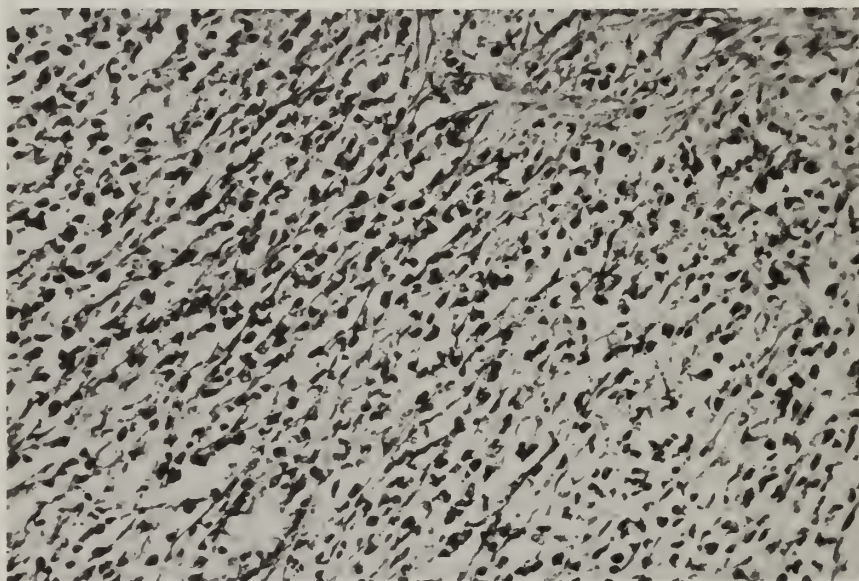


FIG. 2. A—A representative section of one of the many foci of tumor cells infiltrating the muscle layers of the colon. Hematoxylin-eosin, magnification $\times 50$. B—Microscopic studies. Multiple foci of infiltration by the characteristic "signet cells" were noted involving primarily the submucosa and muscularis layers of the colon but also occasionally extending into the lamina propria. The mucosal surface in general was intact. Hematoxylin-eosin, magnification $\times 200$.



LINITIS PLASTICA OF COLON

BASHOUR, GOLDMAN, GERBER AND DANOVITCH

with inflammatory bowel disease, and the lack of local ano-rectal complications (which occur perhaps in 50% of patients with granulomatous colitis^{1,2}, should have alerted us to the possibility that we might not be dealing with granulomatous bowel disease. In addition, the rapid development of colonic obstruction is more characteristic of carcinoma than inflammatory bowel disease. If obstruction had not been present in this case, and if we had procrastinated by treating her with corticosteroids, a lack of clinical improvement also might have made us more suspicious of malignant disease. While Wolff and Marshak¹³ have suggested that a "rigid and fixed appearance" of the bowel segment without clearly demarcated markings may be the earliest and only evidence suggestive of malignancy of the linitis plastica type, other changes such as mucosal effacement, irregular tapering of the lumen, and pseudodiverticulæ (Fig. 1.) are not specific and may indicate either benign or malignant disease^{1,2,5,6,7,8}. Pathologic findings in our case were similar to those reported by others^{1,2,5,6,7,8} and include induration of the pericolic fat, narrowing of the colonic lumen to less than 3 cm. and marked thickening and induration of the wall of the colon and adjacent mesentery with frequent tubo-ovarian extension. Microscopically the characteristic features are the anaplastic, multifocal origin of the tumor and the signet ring cell (Fig. 2B).

We believe that in spite of the rarity of linitis plastica of the colon it must always be considered in the differential diagnosis of atypical, "benign" colonic strictures and when diagnosed, treatment should be wide resection including hysterectomy and bilateral salpingo-oophorectomy.

References

1. LAUFMAN, H., SAPHIR, O.: Primary Linitis Plastica Type of Carcinoma of the Colon. *Arch. Surg.*, 62:70, 1951.
2. TURNBULL, R. B., FISCHER, E. R., ROSENACK, B. D.: Primary Linitis Plastica Carcinoma of the Colon. *Cleveland Clin. Q.*, 18:210, 1951.
3. DIXON, C. F., STEVENS, G. A.: Carcinoma of Linitis Plastica Type Involving Intestine. *Ann. Surg.*, 103:263, 1936.
4. FAHL, J. C., DOCKERTY, M. D., JUDD, E. S.: Scirrhus Carcinoma of the Colon and Rectum. *Surg., Gynec. & Obst.*, 111:759, 1960.
5. ANDERSEN, G. A.: Primary Linitis Plastica of the Colon and Rectum. *Acta Path. Microbiol. Scand.*, 78:277, 1970.
6. NELSON, P. G.: Primary Linitis Plastica of the Colon. *Aust. New Zeal. J. Surg.*, 34:288, 1965.
7. SIZER, J. S., FREDERICK, P. L., OSBORNE, M. P.: Primary Linitis Plastica of the Colon. *Disc. Colon & Rectum*, 10:339, 1967.
8. ANDERSEN, J. A., HANSEN, B. F.: Linitis Plastica of Colon and Rectum. *Disc. Colon Rectum.*, 15:216, 1972.
9. WEINTRAUB, L. R., LITTMAN, L.: Primary Linitis Plastica of the Rectum. *Dis. Colon. Rectum.*, 5:105, 1962.
10. ABADIC, FRANK A., GOODMAN, MAX L.: Linitis Plastica Carcinoma of the Colon. *Arch. Surg.*, 84:687, 1962.
11. FERNET, P., AZAR, H. A., STOUT, A. P.: Intradermal Spread of Linitis Plastica Along the Alimentary Tract. *Gastroenterology*, 48:419, 1965.
12. LINDER, A. E., MARSHAK, R. H., WOLFF, B. S., JANOWITZ, H. D.: Granulomatous Colitis, A Clinical Study. *New Eng. J. Med.*, 269:379, 1963.
13. WOLFF, B. S., MARSHAK, R. H.: Linitis Plastica or Diffusely Infiltrating Type of Carcinoma of the Colon. *Radiology*, 81:502, 1963.
14. WOLFF, B. S., MARSHAK, R. H.: Granulomatous Colitis (Crohn's Disease of the Colon). *Amer. J. Roent.*, 88:662, 1962.

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Syncope Associated with Esophageal Stricture

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Abstract

The second reported case of syncope associated with a hiatal hernia and esophageal stricture is presented. The mechanism is believed to be a vagovagal reflex. Electrocardiographic evidence of complete heart block in association with distention of the esophagus in the region of the stricture was demonstrated by marshmallow barium swallow with EKG monitoring. The symptoms and cardiac changes were blocked by atropine administration. Treatment with long acting anticholinergics and esophageal dilation has prevented further dysphagia or syncope.

Introduction

Syncope related to esophageal dysfunction is not a commonly reported entity. The first case of cardiac syncope associated with esophageal stricture was reported by Tolman and Ashworth¹ in 1971. Their patient had a hiatal hernia with an esophageal stricture and dysphagia, and developed sinus bradycardia with syncope on swallowing. We have had opportunities to study a patient with a sliding hiatal hernia, esophageal stricture, and dysphagia, who developed complete heart

We have had opportunities to study a patient with a sliding hiatal hernia, esophageal stricture, and dysphagia, who developed complete heart block with syncope on swallowing. Atropine was found to prevent the syncopal episodes . . .

block with syncope on swallowing. Atropine was found to prevent the syncopal episodes, and treatment with esophageal dilatation resulted in disappearance of both the dysphagia and the syncope. This report summarizes our findings.

Case Report

W. H., a 54 year old white male attorney, was admitted to the hospital for the first time in March, 1971 with a right occipital linear skull fracture. Just prior to admission, the patient had been hurriedly eating a meal when he experienced an acute attack of dysphagia associated with a sensation of choking. This cause him to rise and drink a glass of water. After finishing the water he suddenly lost consciousness and fell, striking his head on the floor. There was no nausea, retching,

coughing, sweating, vertigo, palpitation, or difficulty in breathing. There also was no seizure activity. The patient regained consciousness within a few seconds and was taken to the hospital, where he complained of slight dizziness and a mild headache. His x-rays showed an occipital fracture and he was admitted for further observation.

The patient had a ten year history of pyrosis, sourbrash, and heartburn which would appear mainly after meals, was worsened by bending or lying down, and was relieved by antacids. There was an eight year history of dysphagia occurring about once a month. It would increase in severity when the patient was under emotional stress. The symptoms would occur primarily on swallowing large pieces of meat or carbonated beverages. For the past two years, there had been syncopal episodes associated with dysphagia occurring approximately four times a year. There was never any associated cough, nausea, vomiting or breathing difficulty. The loss of consciousness never lasted more than a few seconds.

An upper gastrointestinal series two years prior to admission had shown a small hiatal hernia. Esophageal motility studies were normal. Physical examination was entirely within nor-

SYNCOPE ASSOCIATED WITH ESOPHAGEAL STRICTURE

TRUJILLO AND SPERO

mal limits except for a small laceration in the occipital area. Laboratory studies, including a complete blood count, serologic test for syphilis, 12 channel chemistries by autoanalyzer, urinalysis, chest films, and 12 lead EKG were entirely within normal limits. The patient was discharged after an uneventful hospital course.

Approximately two to three months later, evaluation was carried out as follows: a barium study of the esophagus showed a three centimeter sliding hiatal hernia (Figure 1) with narrowing of the esophageal-gastric junction. The stomach and duodenum were normal. A marshmallow barium swallow was obtained (Figure 2) with EKG monitoring. Under fluroscopic observation, the marshmallow was seen to stop forward motion at the area of the stricture, and at this time the patient's unconsciousness was reproduced. An EKG recording at this instant showed a complete heart block (Figure 3). This response was reversed with 0.4 milligrams of atropine. At esophagoscopy, with prior medication with atropine, an esophageal stricture approximately 1.2 centimeters in width was found at the esophago-gastric junction.

The patient was dilated to 54 French with Hurst rubber dilators. He has been followed for a year and a half, receiving long acting anticholinergics during the day. There have been no further episodes of dysphagia or syncope. Re-endoscopy 16 months later showed that the diameter of the stricture had remained at approximately 18 millimeters.

Comments

In 1934, Weiss and Ferris² described the first reported case of syncope associated with an esophageal abnormality. Their patient showed transient complete heart block and syncope on swallowing. An esophageal



FIG. 1. A barium study of the esophagus showed a three centimeter sliding hiatal hernia with narrowing of the esophageal-gastric junction.

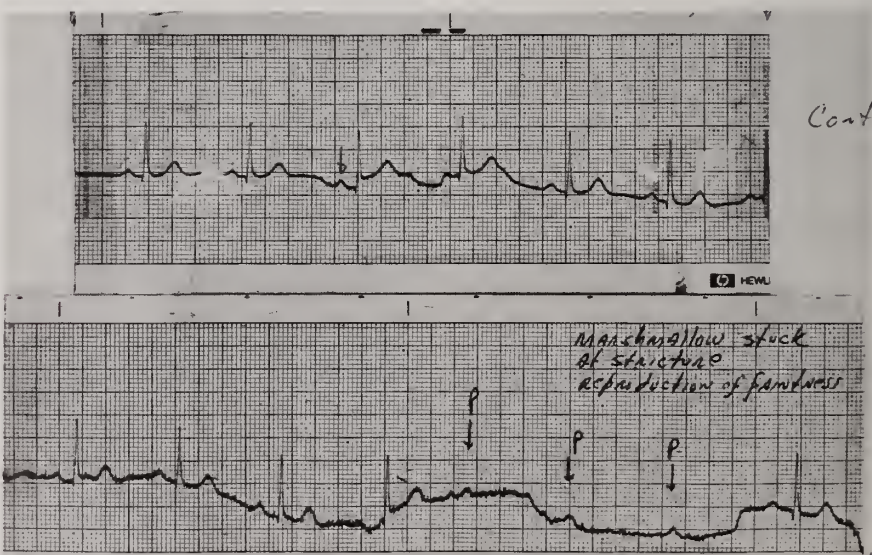


FIG. 3. The marshmallow was seen to stop forward motion at the area of the stricture, and the patient's unconsciousness was reproduced. An EKG recording showed a complete heart block.



FIG. 2. A marshmallow barium swallow was obtained with EKG monitoring.

diverticulum was found to be present and may have been responsible for the cardiac abnormality. Administration of atropine and vagal infiltration high in the neck completely abolished the heart block and syncope. It was postulated that a vago-vagal reflex was responsible for the heart block. The initial stimulus was thought to be esophageal distention at the site of the diverticulum. These findings were reproduced by balloon distention of the esophagus.

Morrison and Swalm³ experimentally produced heart block and syncope, in a patient suffering from angina pectoris, by inflating a balloon in the stomach. Others have reported syncope associated with esophageal abnormalities^{4,5,6} in patients who have been digitalized. Regaza, Rectra and Pardi⁷ reported intermittent complete heart block associated with swallowing in a patient who had suffered an acute myocardial infarction. The role of diffuse esophageal spasm in initiating syncopal attack was elucidated by Kopald⁸ using manometric and cine-radiographic studies.

In all of the above cases, the reflex thought to be responsible for the syncopal attacks was vagovagal, with the afferent limb originating in an abnormal esophagus. Arteriosclerotic heart disease, a damaged myocardium, a diseased conduction system, and digitalis were all shown to potentiate the reflex. There are those who dispute the belief that both afferent and efferent pathways are vagal in nature, and who state that formal proof is lacking to pinpoint the vagus nerve as the sole afferent limb⁹.

Syncope in association with an esophageal abnormality is a distinct but rare entity, and may exist independently of heart disease or digitalis use. Our patient showed heart block producing syncope in response to distention of his esophagus by a marshmallow in the region of a stric-

SYNCOPE ASSOCIATED WITH ESOPHAGEAL STRICTURE

TRUJILLO AND SPERO

ture. Although the patient reported by Tolman¹ showed syncopal attack in association with the same esophageal abnormality their patient's cardiac response was that of sinus bradycardia rather than complete heart block. It does appear, however, that vagal influence is of import in the etiology of both these responses. Treatment with esophageal dilatation and anticholinergics has been effective in both cases in preventing further syncopal episodes.

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References

1. TOLMAN, K. G., ASHWORTH, W. D.: Syncope Induced Dysphagia, Correction by Esophageal Dilatation. *Digestive Diseases*, 16:1026, 1971.
2. WEISS, S., FERRIS, E. B.: Adams-Stokes Syndrome with Transient Complete Heart Block of Vagovagal Reflex Origin. *Arch. Internal Medicine* 54:931, 1934.
3. MORRISON, L. M., SWALM, W. A.: Role of the Gastrointestinal Tract in Production of Cardiac Symptoms. *JAMA*, 114:217, 1940.
4. LICHSTEIN, E., CHADDA: Atrioventricular Block Produced by Swallowing, with Documentation by His Bundle Recordings. *American Journal of Cardiology*, 29:561, 1972.
5. CORRELL, H. L., LINDERT, M. C. F.: Vagovagal Syncope, Report of a Case Apparently Induced by Digitalization. *American Heart Journal*, 37:446, 1949.
6. JAMES, A. H.: Cardiac Syncope After Swallowing. *Lancet*, 1:771, 1958.
7. RAGAZA, E. P., RECTRA, E. H., PARDI, M. T.: Intermittent Complete Heart Block Associated with Swallowing as a Complication of Acute Myocardial Infarction. *American Heart Journal*, 79:396, 1970.
8. KOPALD, H. H., *et al*: Vagovagal Syncope. Report of a Case Associated with Diffuse Esophageal Spasm. *New England Journal of Medicine*, 271:1238, 1964.
9. SAPRU, R. P. *et al*: Syncope on Swallowing. *British Heart Journal*, 33:617, 1971.
10. TOLMAN, K. G., ASHWORTH, W. D.: Syncope Induced by Dysphagia, Correction by Esophageal Dilatation. *Digestive Diseases*, 16:1026, 1971.



What does man have in common with Samson?

Neither man nor the gorilla can synthesize vitamin C. Interestingly, the slow loris, a primate much further down the evolutionary scale, can convert L-1,4-gulonolactone to ascorbic acid in its liver and presumably does not require an exogenous source of ascorbic acid.

Because man can neither synthesize vitamin C nor store most of the water soluble vitamins, these nutrients must be replenished continuously in order to

maintain normal tissue levels.

Generally, this is accomplished in his daily diet. But under conditions of illness, stress, in convalescence or following surgery, vitamin stores may be depleted or metabolic demands increased.

In such cases, Surbex-T may be indicated. Surbex-T restores the water-soluble vitamins with each tablet providing 500 mg. of vitamin C plus high potency B-complex.



SURBEX-T[®] 500 mg. of Vitamin C with High Potency B-Complex
Restores what the body cannot effectively store

When diarrhea wrings the wedding belle...

It's all very well to counsel patience in diarrhea patients. There are times when relief of symptoms can't come too soon.

X-ray studies¹ in 16 normal subjects showed just how promptly the active ingredient in Lomotil does its work.

Lomotil retarded gastrointestinal motility particularly during the first three hours after administration. It continued its moderating action on the bowel for at least three hours more.

Physicians prescribe Lomotil more often than any other drug when the urgency for the control of diarrhea is most distressing.

1. Demeulenaere, L.: Action du R 1132 sur le transit gastro-intestinal, *Acta Gastroent. Belg.* 21:674-680 (Sept.-Oct.) 1958.

Lomotil[®]

TABLETS/LIQUID

Each tablet and each 5 ml. of liquid contain:

diphenoxylate hydrochloride . . . 2.5 mg.

(Warning: May be habit-forming)

atropine sulfate 0.025 mg.

Saves the Day





IMPORTANT INFORMATION: This is a Schedule V substance by Federal law; diphenoxylate HCl is chemically related to meperidine. In case of overdose or individual hypersensitivity, reactions similar to those after meperidine or morphine overdose may occur; treatment is similar to that for meperidine or morphine intoxication (prolonged and careful monitoring). Respiratory depression may recur in spite of an initial response to Nalline® (nalorphine HCl) or may be evidenced as late as 30 hours after ingestion. LOMOTIL IS NOT AN INNOCUOUS DRUG AND DOSAGE RECOMMENDATIONS SHOULD BE STRICTLY ADHERED TO, ESPECIALLY IN CHILDREN. THIS MEDICATION SHOULD BE KEPT OUT OF REACH OF CHILDREN.

Indications: Lomotil is effective as adjunctive therapy in the management of diarrhea.

Contraindications: In children less than 2 years, due to the decreased safety margin in younger age groups, and in patients who are jaundiced or hypersensitive to diphenoxylate HCl or atropine.

Warnings: Use with caution in young children, because of variable response, and with extreme caution in patients with cirrhosis and other advanced hepatic disease or abnormal liver function tests, because of possible hepatic coma. Diphenoxylate

HCl may potentiate the action of barbiturates, tranquilizers and alcohol. In theory, the concurrent use with monoamine oxidase inhibitors could precipitate hypertensive crisis.

Usage in pregnancy: Weigh the potential benefits against possible risks before using during pregnancy, lactation or in women of childbearing age. Diphenoxylate HCl and atropine are secreted in the breast milk of nursing mothers.

Precautions: Addiction (dependency) to diphenoxylate HCl is theoretically possible at high dosage. Do not exceed recommended dosages. Administer with caution to patients receiving addicting drugs or known to be addiction prone or having a history of drug abuse. The subtherapeutic amount of atropine is added to discourage deliberate overdose; strictly observe contraindications, warnings and precautions for atropine; use with caution in children since signs of atropinism may occur even with the recommended dose.

Adverse reactions: Atropine effects include dryness of skin and mucous membranes, flushing and urinary retention. Other side effects with Lomotil include nausea, sedation, vomiting, swelling of the gums, abdominal discomfort, respiratory depression, numbness of the extremities, headache, dizziness, depression, malaise, drowsiness, coma, lethargy, anorexia, restlessness, euphoria, pruritus, angioneurotic edema, giant urticaria and paralytic ileus.

Dosage and administration: Lomotil is contraindicated in children less than 2 years old. Use only Lomotil liquid for children 2 to 18 years old. For

ages 2 to 5 years, 4 ml. (2 mg.) t.i.d.; 5 to 8 years, 4 ml. (2 mg.) q.i.d.; 8 to 12 years, 4 ml. (2 mg.) 5 times daily; adults, two tablets (5 mg.) t.i.d. to two tablets (5 mg.) q.i.d. or two regular teaspoonfuls (10 ml., 5 mg.) q.i.d. Maintenance dosage may be as low as one fourth of the initial dosage. Make downward dosage adjustment as soon as initial symptoms are controlled.

Overdose: Keep the medication out of the reach of children since accidental overdose may cause severe, even fatal, respiratory depression. Signs of overdose include flushing, lethargy or coma, hypotonic reflexes, nystagmus, pinpoint pupils, tachycardia and respiratory depression which may occur 12 to 30 hours after overdose. Evacuate stomach by lavage, establish a patent airway and, when necessary, assist respiration mechanically. Use a narcotic antagonist in severe respiratory depression. Observation should extend over at least 48 hours.

Dosage forms: Tablets, 2.5 mg. of diphenoxylate HCl with 0.025 mg. of atropine sulfate. Liquid, 2.5 mg. of diphenoxylate HCl and 0.025 mg. of atropine sulfate per 5 ml. A plastic dropper calibrated in increments of ½ ml. (total capacity, 2 ml.) accompanies each 2-oz. bottle of Lomotil liquid.

SEARLE

Searle & Co.
San Juan, Puerto Rico 00936

Address medical inquiries to:
G. D. Searle & Co.
Medical Department, Box 5110,
Chicago, Illinois 60680

Sign of a cold* sufferer

Time for Ornade®

Each Spansule® capsule contains 8 mg. Teldrin® (brand of chlorpheniramine maleate); 50 mg. phenylpropanolamine hydrochloride; 2.5 mg. isopropamide, as the iodide.

Fast relief of upper respiratory congestion and hypersecretion* with convenient b.i.d. dosage.

Before prescribing, see complete prescribing information in SK&F literature or PDR. The following is a brief summary.

Indications

Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

Possibly effective: For relief of upper respiratory tract congestion and hypersecretion associated with vasomotor rhinitis and allergic rhinitis, and for prolonged relief.

Lacking in substantial evidence of effectiveness: For relief of nasal congestion and hypersecretion associated with the common cold and sinusitis.

Final classification of the less-than-effective indications requires further investigation.

Contraindications: Hypersensitivity to any component; concurrent MAO inhibitor therapy; severe hypertension; bronchial asthma; coronary artery disease; stenosing peptic ulcer; pyloroduodenal or bladder neck obstruction. Children under 6.

Warnings: Caution patients about activities requiring alertness (e.g., operating vehicles or machinery). Warn patients of possible additive effects with alcohol and other CNS depressants.

Usage in Pregnancy: In pregnancy, nursing mothers and women who might bear children, weigh potential benefits against hazards. Inhibition of lactation may occur.

Effect on PBI Determination and I^{131} Uptake: Isopropamide iodide may alter PBI test results and will suppress I^{131} uptake. Substitute thyroid tests unaffected by exogenous iodides.

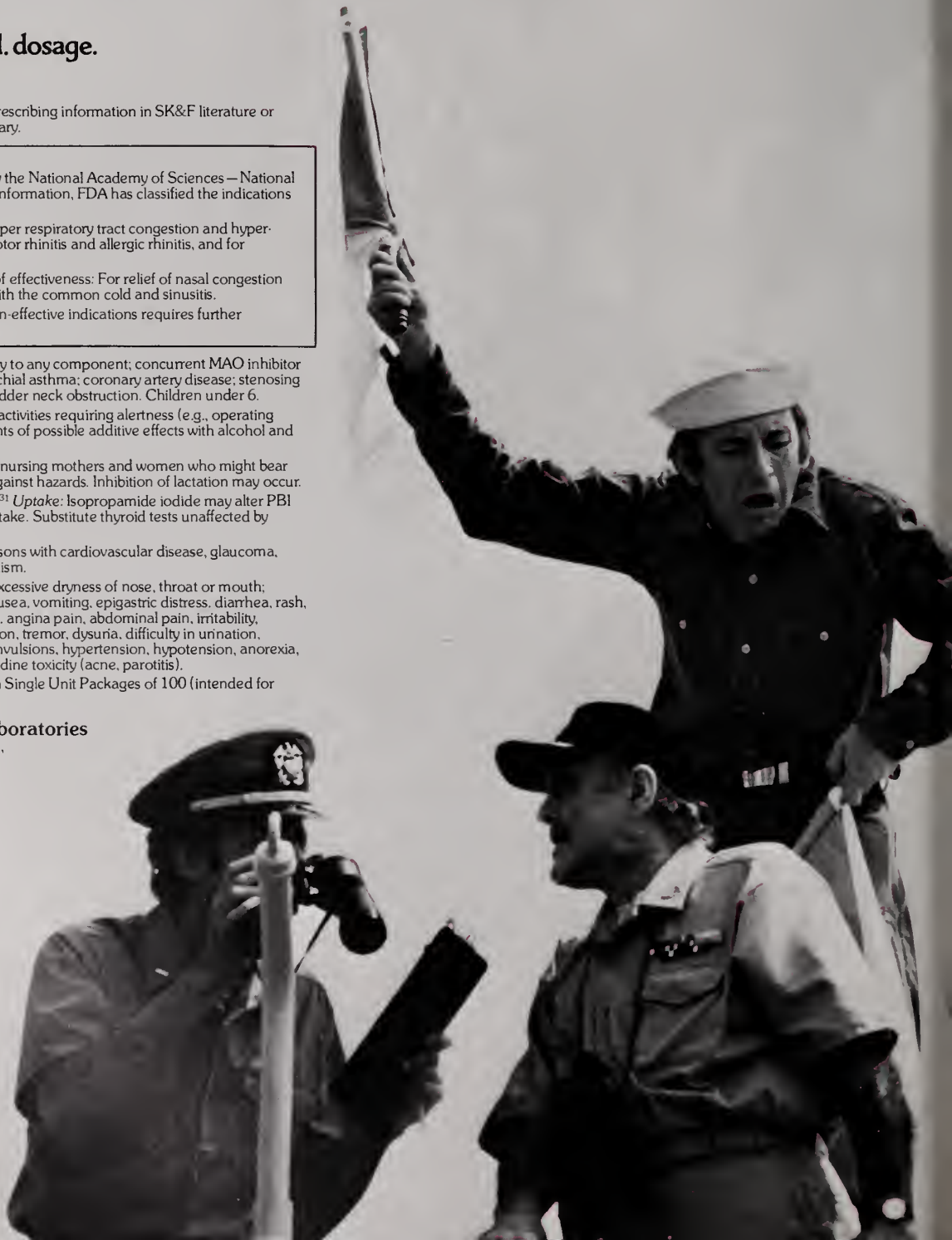
Precautions: Use cautiously in persons with cardiovascular disease, glaucoma, prostatic hypertrophy, hyperthyroidism.

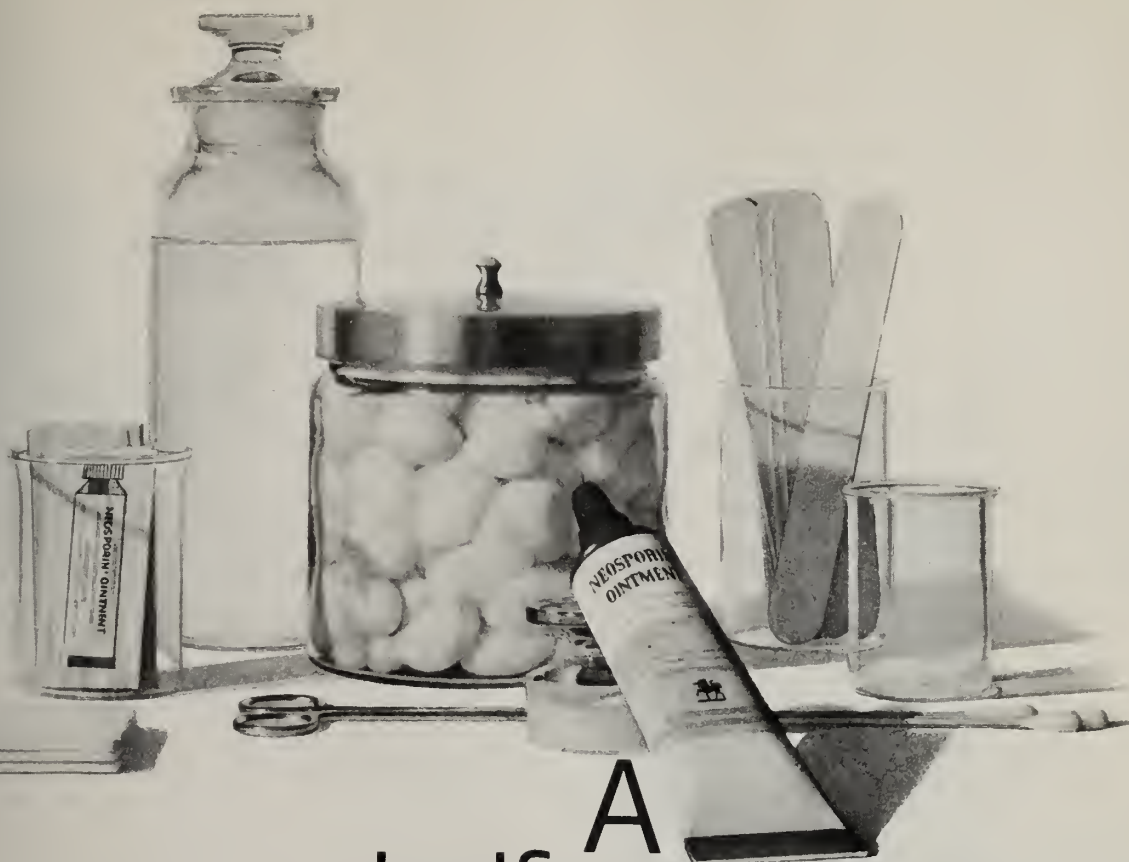
Adverse Reactions: Drowsiness, excessive dryness of nose, throat or mouth; nervousness; or insomnia. Also, nausea, vomiting, epigastric distress, diarrhea, rash, dizziness, weakness, chest tightness, angina pain, abdominal pain, irritability, palpitation, headache, incoordination, tremor, dysuria, difficulty in urination, thrombocytopenia, leukopenia, convulsions, hypertension, hypotension, anorexia, constipation, visual disturbances, iodine toxicity (acne, parotitis).

Supplied: Bottles of 50 capsules; in Single Unit Packages of 100 (intended for institutional use only).

Smith Kline & French Laboratories

Division of SmithKline Corporation,
Philadelphia, Pa. 19101





A half-ounce of prevention

Use it to prevent a topical infection. Or to treat one that's already started.

In either case, it's good medicine. Whether for lacerations, burns, open wounds, IV catheter or surgical aftercare.

Neosporin® Ointment provides broad antibacterial coverage against common susceptible pathogens. And since it contains three antibiotics that are rarely used systemically, the risk of sensitization is reduced.

Neosporin Ointment. A half-ounce of prevention. Also available in a full ounce of prevention and in convenient foil packets.

Neosporin Ointment carried on Apollo and Skylab missions.

Neosporin® Ointment (polymyxin B-bacitracin-neomycin)

Each gram contains: Aerosporin® brand Polymyxin B Sulfate 5,000 units; zinc bacitracin 400 units; neomycin sulfate 5 mg (equivalent to 3.5 mg neomycin base); special white petrolatum qs.
In tubes of 1 oz and 1/2 oz and 1/32 oz (approx.) foil packets.

INDICATIONS: *Therapeutically*, used as an adjunct to appropriate systemic therapy for topical infections, primary or secondary, due to susceptible organisms, as in: • infected burns, skin grafts, surgical incisions, otitis externa • primary pyodermas (impetigo, ecthyma, sycosis vulgaris, paronychia) • secondarily infected dermatoses (eczema, herpes, and seborrheic dermatitis) • traumatic lesions, inflamed or suppurating as a result of bacterial infection. *Prophylactically*, the ointment may be used to prevent bacterial contamination of burns, skin grafts, incisions, and other clean lesions. For abrasions, minor cuts and wounds accidentally incurred, its use may prevent the development of infection and permit wound healing.

CONTRAINDICATIONS: Not for use in the eyes or external ear canal if the eardrum is perforated. This product is contraindicated in those individuals who have known hypersensitivity to any of the components.

WARNING: Because of the potential hazard of nephrotoxicity and ototoxicity associated with neomycin, care should be exercised when using this product in treating

absorption of neomycin is possible. In burns where more than 20 percent of the body surface is affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended.

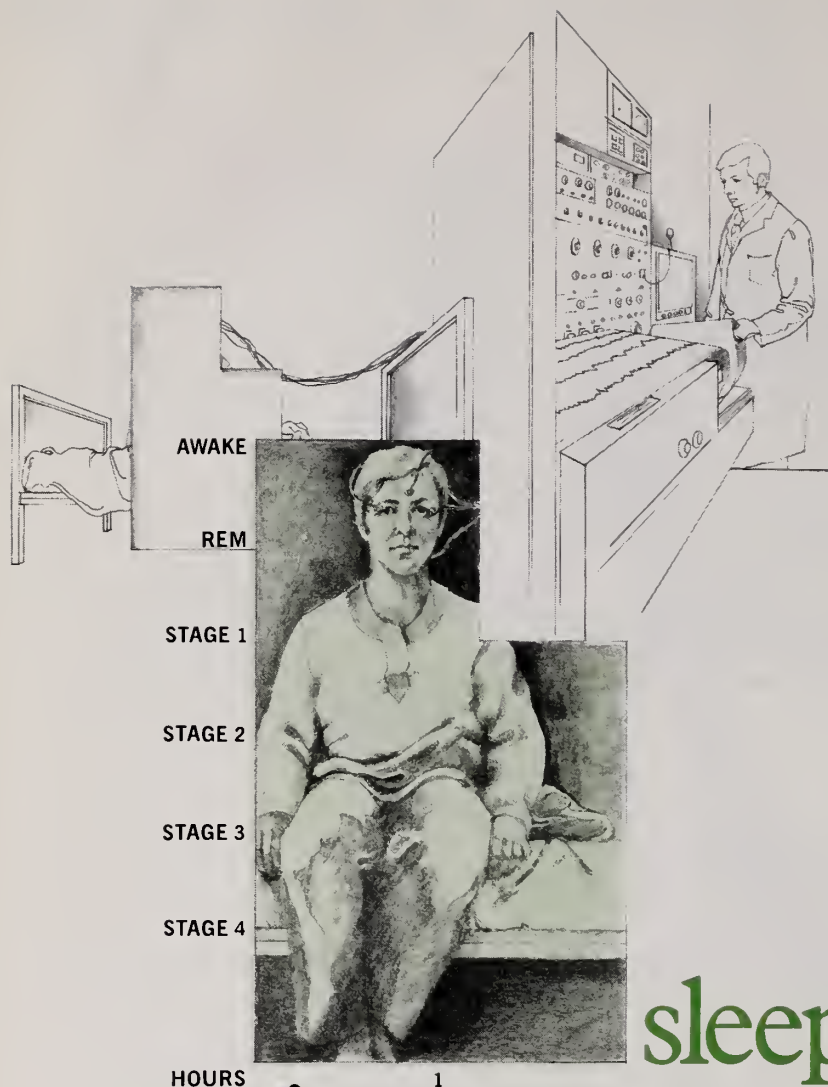
PRECAUTIONS: As with other antibacterial preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs.

ADVERSE REACTIONS: Neomycin is a not uncommon cutaneous sensitizer. Articles in the current literature indicate an increase in the prevalence of persons allergic to neomycin. Ototoxicity and nephrotoxicity have been reported (see Warning section).

Complete literature available on request from Professional Services Dept. PML.



Burroughs Wellcome Co.
Research Triangle Park

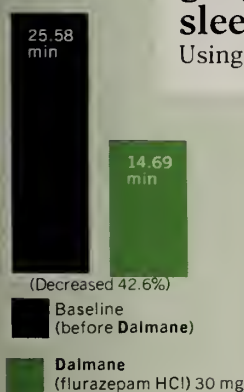


sleep
begins within
17 minutes, on average ...
an initial benefit of

Dalmane[®]
(flurazepam HCl) proved by a
22-night clinical study of insomnia patients
in the sleep research laboratory and at home¹

Three insomnia patients selected for difficulty falling asleep were administered Dalmane (flurazepam HCl) 30 mg for 14 consecutive nights. Placebo was given for four nights prior to and four nights after Dalmane. Physiologic tracings on Dalmane nights 1-3 showed sleep induction time averaged 13.90 minutes; on Dalmane nights 12-14, 18.80 minutes. Combined average for the 6 monitored drug nights was 16.35 minutes.¹

Average Time Required
to Fall Asleep (4 Studies,
16 Subjects²⁻⁴)



confirmed by clinical studies in four geographically separated sleep research laboratories²⁻⁵

Using a 14-night protocol involving eight insomniac and eight normal subjects, four studies confirmed the sleep-inducing effectiveness of Dalmane (flurazepam HCl) and the reproducibility of this response. On average, one 30-mg capsule induced sleep within 17 minutes. In all these studies, Dalmane induced sleep rapidly, reduced nighttime awakenings, and provided 7 to 8 hours of sleep without repeating dosage²⁻⁵

Dalmane (flurazepam HCl) induces and maintains sleep, with relative safety

Dalmane is generally well tolerated; morning "hang-over" has been relatively infrequent. While dizziness, drowsiness, lightheadedness and the like have been noted most often, particularly in the elderly and debilitated, physicians should be aware of the possibility of more serious reactions, as noted below.

Before prescribing Dalmane (flurazepam HCl), please consult Complete Product Information, a summary of which follows:

Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening; in patients with recurring insomnia or poor sleeping habits; and in acute or chronic medical situations requiring restful sleep. Since insomnia is often transient and intermittent, prolonged administration is generally not necessary or recommended.

Contraindications: Known hypersensitivity to flurazepam HCl.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Use in women who are or may become pregnant only when potential benefits have been weighed against possible hazards. Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated, initial dosage should be limited to 15 mg to preclude oversedation, dizziness and/or ataxia. If combined with other drugs having hypnotic or CNS-depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with latent depression or suicidal tendencies. Periodic blood counts and liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdose, have been reported. Also reported were headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins and alkaline phosphatase. Paradoxical reactions, e.g., excitement, stimulation and hyperactivity, have also been reported in rare instances.

Dosage: Individualize for maximum beneficial effect. *Adults:* 30 mg usual dosage; 15 mg may suffice in some patients. *Elderly or debilitated patients:* 15 mg initially until response is determined.

Supplied: Capsules containing 15 mg or 30 mg flurazepam HCl.

when restful sleep
is indicated

Dalmane[®]

(flurazepam HCl)

One 30-mg capsule h.s. — usual adult dosage
(15 mg may suffice in some patients).

One 15-mg capsule h.s. — initial dosage for elderly or debilitated patients.

- induces sleep within 17 minutes, on average
- reduces nighttime awakenings
- sustains sleep 7 to 8 hours, on average, without repeating dosage



ROCHE LABORATORIES
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

REFERENCES: 1. Kales A, et al: *Arch Gen Psychiatry* 23:226-232, Sep 1970

2. Karacan I, Williams RL, Smith JR: The sleep laboratory in the investigation of sleep and sleep disturbances. Scientific exhibit at the 124th annual meeting of the American Psychiatric Association, Washington DC, May 3-7, 1971

3. Frost JD Jr: Data on file, Medical Department, Hoffmann-La Roche Inc, Nutley NJ

4. Vogel GW: Data on file, Medical Department, Hoffmann-La Roche Inc, Nutley NJ

5. Dement WC: Data on file, Medical Department, Hoffmann-La Roche Inc, Nutley NJ

The Role of the Detail Man

"I may be prejudiced, but I am very much in favor of the detail men I meet. Most of them are knowledgeable about the drugs they promote and can be a great help in acquainting me with new medication."

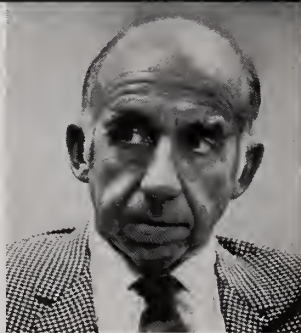
Family Physician's Perception

I think that most general practitioners in this area feel as I do about the detail man. Over the years I have gotten to know most of the men who visit me regularly and they in turn have become aware of my particular interests and the nature of my practice. They, therefore, limit their discussion as much as possible to the areas of interest to me. Since I usually see the same representative again in future visits, it is in his best interest to supply me with the most honest, factual, as well as up-to-date information about his products.

Dr. Willard Gobbell
Family Physician
Encino, California



Dr. Jeremiah Stamler
Chairman
Department of Community
Health and Preventive
Medicine, and Dingman
Professor of Cardiology
Northwestern University
Medical School



"In the total picture of dealing with health problems in this country, there is a potential for detail men to play a meaningful role."

The Positive Influence

My contact with representatives and salesmen of the pharmaceutical industry is the type of contact that people in a medical center, research people, and academic people have and that's in all likelihood on a somewhat different level from that of the practicing physician.

Let me touch on how I personally perceive the role of the sales representative. These men reach large numbers of health professionals. Thus they could be—and at times actually are—disseminators of useful information. They could consistently serve a real educational function in their ability to discuss their products.

At present they do distribute printed material, brochures and pamphlets—some of it scientifically sound and therefore truly useful—as well as some excellent films produced by the pharmaceutical industry. When they function in this

Opinion
&
Dialogue

Is He a Source of Information?

Yes, with certain reservations. The average sales representative has a great fund of information about the drug products he is responsible for. He is usually able to answer most questions fully and intelligently. He can also supply reprints of articles that contain a great deal of information. Here, too, I exercise some caution. I usually accept most of the statements and opinions that I find in the papers and studies which come from the larger teaching facilities. It goes without saying that a physician should also rely on other sources for his information on pharmacology.

Training of Sales Representatives

Ideally, a candidate for the position as a sales representative of a pharmaceutical company should be a graduate pharmacist who has a questioning mind. I don't think this is possible in every case, and so it becomes the responsibility

of the pharmaceutical company to train these individuals comprehensively. It is of very great importance that the detail man's knowledge of the product he represents be constantly reviewed as well as updated. This phase of the sales representative's education should be a major responsibility of the medical department of the pharmaceutical company.

I am certain that most of these companies take special care to give their detail men a great deal of information about the products they produce — information about indications, contraindications, side effects and precautions. Yet, although most of the detail men are well informed, some, unfortunately, are not. It might be helpful if sales representatives were reassessed every few years to determine whether or not they are able to fulfill their important function. Incidentally, I feel the same way about periodic assessments of everyone

in the health care field, whether they be general practitioners, surgeons or salesmen.

Value of Sampling

I personally am in favor of limited sampling. I do not use sampling in order to perform clinical testing of a drug. I feel that drug testing should rightly be left to the pharmacology researcher and to the large teaching institutions where such testing can be done in a controlled environment.

I do not use samples as a "starter dose" for my patients. I do, however, find samples of drugs to be of value in that they permit me to see what the particular medication looks like. I get to see the various forms of the particular medication at first hand, and if it is in a liquid form I take the time to taste it. In that way I am able to give my patients more complete information about the particular medications that I prescribe for them.

capacity they are indeed useful; particularly in the fact that they disseminate broadly based educational material and serve not just as "pushers" of their drugs.

The Other Side of the Coin

Obviously, the pharmaceutical companies are not producing all this material as a labor of love — they are in the business of selling products for profit. In this regard the ambitious and improperly motivated sales representative can exert a negative influence on the practicing physician, both by presenting a one-sided picture of his product, and by encouraging the practitioner to depend too heavily on drugs for his total therapy. In these ways, the salesman has often distorted objective reality and undermined his potential role as an educator.

The Industry Responsibility

Since the detail man must be an information resource as well as a representative of his particular pharmaceutical company, he should be carefully selected and

thoroughly trained. That training, perforce, must be an ongoing one. There must be a continuing battle within and with the pharmaceutical industry for high quality not only in the selection and training of its sales representatives, but also in the development of all of its promotional and educational material.

The industry must be ready to accept constructive as well as corrective criticism from experts in the field and consumer spokesmen, and be willing to accept independent peer review. The better educated and prepared the salesman is, the more medically accurate his materials, the better off the pharmaceutical industry, health professionals and the public — i.e., the patients — will be.

Physician Responsibility

The practicing physician is in constant need of up-dated information on therapeutics, including drugs. He should and does make use of drug information and answers to specific questions supplied by the pharmaceutical representative. However, that informa-

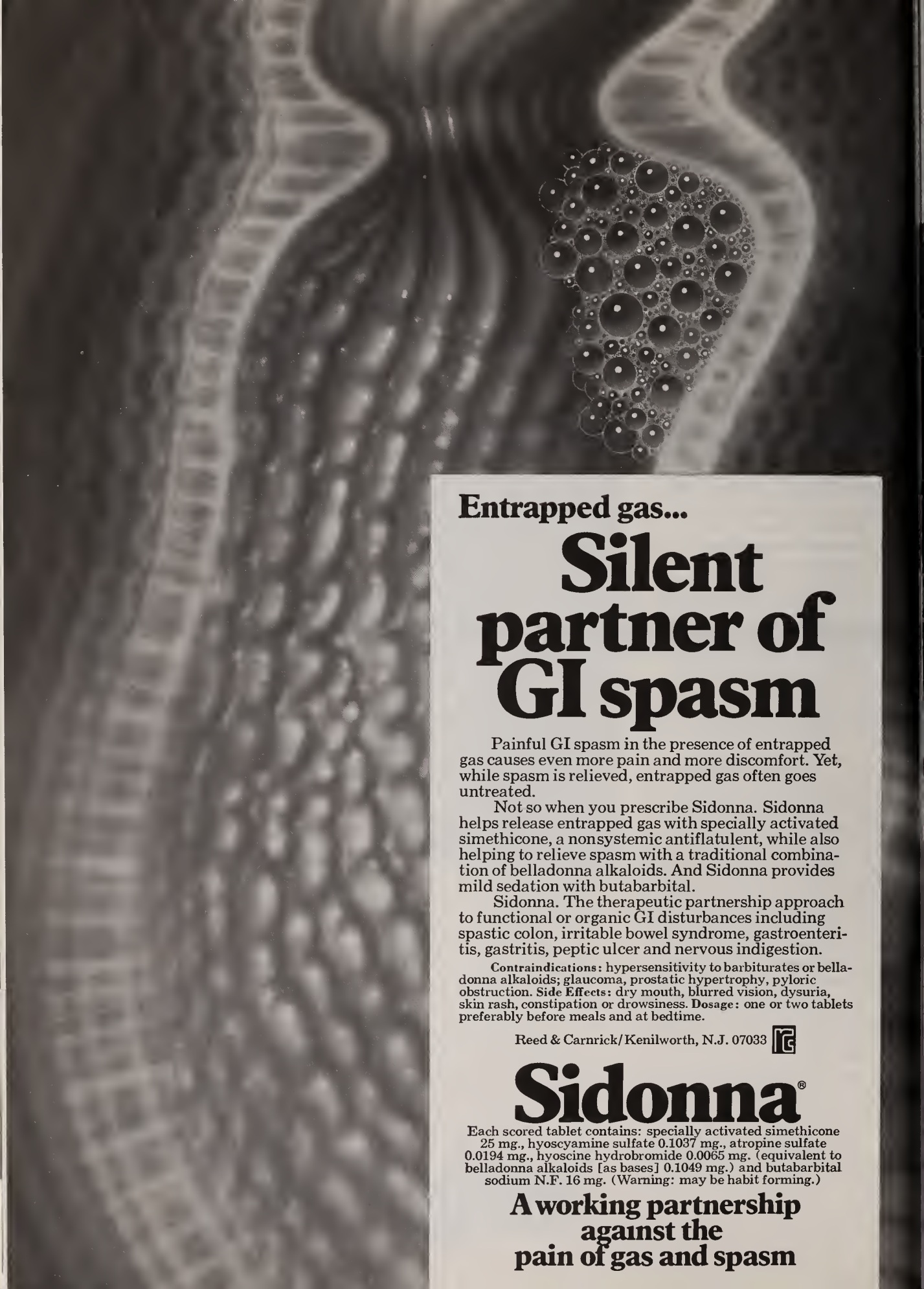
tion must not be his main source of continuing education. The practitioner must keep up with what is current by making use of scientific journals, refresher courses, and information received at scientific meetings.

The practicing physician not only has the right, but has the responsibility to demand that the pharmaceutical company and its representatives supply a high level of valid and useful information. I feel certain that if such a high level is demanded by the physician as well as the public, this demand will be met by an alert and concerned pharmaceutical industry.

From my experience, my impression is that sectors of the pharmaceutical industry are indeed ethical. I challenge the industry as a whole to live up to that word in its finest sense.

Pharmaceutical
Manufacturers Association
1155 Fifteenth Street, N.W.
Washington, D. C. 20005





Entrapped gas...

Silent partner of GI spasm

Painful GI spasm in the presence of entrapped gas causes even more pain and more discomfort. Yet, while spasm is relieved, entrapped gas often goes untreated.

Not so when you prescribe Sidonna. Sidonna helps release entrapped gas with specially activated simethicone, a nonsystemic antiflatulent, while also helping to relieve spasm with a traditional combination of belladonna alkaloids. And Sidonna provides mild sedation with butabarbital.

Sidonna. The therapeutic partnership approach to functional or organic GI disturbances including spastic colon, irritable bowel syndrome, gastroenteritis, gastritis, peptic ulcer and nervous indigestion.

Contraindications: hypersensitivity to barbiturates or belladonna alkaloids; glaucoma, prostatic hypertrophy, pyloric obstruction. **Side Effects:** dry mouth, blurred vision, dysuria, skin rash, constipation or drowsiness. **Dosage:** one or two tablets preferably before meals and at bedtime.

Reed & Carnrick/Kenilworth, N.J. 07033 

Sidonna®

Each scored tablet contains: specially activated simethicone 25 mg., hyoscyamine sulfate 0.1037 mg., atropine sulfate 0.0194 mg., hyoscine hydrobromide 0.0065 mg. (equivalent to belladonna alkaloids [as bases] 0.1049 mg.) and butabarbital sodium N.F. 16 mg. (Warning: may be habit forming.)

**A working partnership
against the
pain of gas and spasm**

The Rx that says "Relax"



BUTISOL Sodium provides highly predictable sedative effect:

minor dosage adjustments are usually all that's needed to produce the desired degree of sedation. (With 3 dosage forms and 4 strengths to make adjustments easy.)

BUTISOL Sodium offers prompt, smooth, relatively non-cumulative action:

begins to work within 30 minutes... yet, because of its intermediate rate of metabolism, generally has neither a "roller-coaster" nor a "hangover" effect.

BUTISOL Sodium is remarkably well tolerated:

a 30-year safety record assures you that there is little likelihood of unexpected reactions.

BUTISOL Sodium saves your patients money:

costs less than half as much as most commonly prescribed sedative tranquilizers.*

These are four good reasons for prescribing BUTISOL Sodium for the many patients who need to have the pace set just a little slower. Its gentle daytime sedative action is often all that's needed to help the usually well-adjusted patient cope with temporary stress.

*Based on surveys of average daily prescription costs.

Butisol  **SODIUM**
(SODIUM BUTABARBITAL)

Contraindications: Sensitivity or idiosyncrasy to barbiturates; history of manifest or latent porphyria or marked liver impairment; respiratory disease with dyspnea or obstruction; history of addiction to sedative/hypnotic drugs; uncontrolled pain, to avoid because of possible excitement.

Precautions: Exercise caution in: moderate to severe hepatic disease; anticoagulant therapy, because of possible increased metabolism of coumarin anticoagulants; withdrawal in drug dependence or the taking of excessive doses over a long period, to avoid withdrawal symptoms; elderly or debilitated patients, to avoid possible marked excitement or depression; use with alcohol or other CNS depressants, because of combined effects.

Adverse Reactions: Slight hangover, drowsiness, lethargy, headache, skin eruptions, nausea and vomiting, hypersensitivity reactions (especially in those with asthma, urticaria, angioneurotic edema, or similar conditions).

Usual Adult Dosage: For daytime sedation, 15 mg. to 30 mg. t.i.d. or q.i.d. For hypnosis, 50 mg. to 100 mg.

Available as: Tablets, 15 mg., 30 mg., 50 mg., 100 mg.; Elixir, 30 mg. per 5 cc. (alcohol 7%). BUTICAPS® [Capsules BUTISOL SODIUM (sodium butabarbital)] 15 mg., 30 mg., 50 mg., 100 mg.

McNEIL

McNeil Laboratories, Inc., Fort Washington, Pa. 19034

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Blowing the whistle on the \$2 billion health boondoggle.



Fad diets, fountains of youth, sex rejuvenators, worthless cancer and arthritis "cures," unscientific cults—every year Americans waste at least \$2 billion on such fraudulent and often dangerous health products and practices.

Who blows the whistle on them? Who helps expose them to the public? Often, it's the AMA. The AMA is the largest collector and disseminator of information on health frauds in this country, serving as the clearing-house of such information for federal, state and municipal agencies and the public. It also provides regulatory and law enforcement agencies with documentation of such frauds for use in prosecution.

Physicians often ask what the AMA does. Protecting Americans from health frauds is just one of its many activities -- all made possible by the physicians who support the AMA through their membership. Find out more about the AMA and how it serves the public and the profession. Just send in the completed coupon.

**Join us.
We can do much more together.**

Dept. D W
American Medical Association
535 N. Dearborn St.
Chicago, Ill. 60610



Please send me more information on
the AMA and AMA membership.

Name

Address

City/State/Zip

IN COUGHS OF COLDS, 'FLU' AND U.R.I.- CLEAR THE TRACT WITH THE ROBITUSSIN[®] LINE

Fall and winter coughs are back. Time to help clear the lower respiratory tract with the five Robitussins and Cough Calmers. All contain glyceryl guaiacolate, the efficient expectorant that works systemically to help increase the output of lower respiratory tract fluid. The enhanced flow of less viscid secretions soothes the tracheo-bronchial mucosa, promotes ciliary action, and makes thick, inspissated mucus less viscid and easier to raise. Available on your prescription or recommendation.

For unproductive coughs

ROBITUSSIN[®]

Each 5 cc. contains:

Glyceryl guaiacolate 100 mg.
Alcohol, 3.5%

For severe coughs

ROBITUSSIN A-C[®] ☾

Each 5 cc. contains:

Glyceryl guaiacolate 100 mg.
Codeine phosphate 10.0 mg.
(warning: may be habit forming)
Alcohol, 3.5%

Non-narcotic for 6-8 hr. cough control

ROBITUSSIN-DM[®]

Each 5 cc. contains:

Glyceryl guaiacolate 100 mg.
Dextromethorphan hydrobromide 15 mg.
Alcohol, 1.4%

Robitussin-DM in solid form for "coughs on the go"

COUGH CALMERS[®]

Each Cough Calmer contains:

Glyceryl guaiacolate 50 mg.
Dextromethorphan hydrobromide 7.5 mg.

Clears nasal and sinus passages as it relieves coughs

ROBITUSSIN-PE[®]

Each 5 cc. contains:

Glyceryl guaiacolate 100 mg.
Phenylephrine hydrochloride 10 mg.
Alcohol, 1.4%

MEET THE NEWEST MEMBER OF THE LINE

Comprehensive decongestant action helps control cough and clear stuffy nose and sinuses. Non-narcotic.

ROBITUSSIN[®]-CF

Each 5 cc. contains:

Glyceryl guaiacolate 50 mg.
Dextromethorphan hydrobromide 10.0 mg.
Phenylpropanolamine hydrochloride 12.5 mg.
Alcohol, 1.4%

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The more physicians consider the hemodynamics of lowering blood pressure...

Most physicians now agree on the importance of reducing blood pressure in the hypertensive patient. But high blood pressure exists, of course, only as part of a complete clinical picture. The hemodynamic profile of well-established essential hypertension is characterized by elevated arterial blood pressure, normal cardiac output, and increased total peripheral resistance.

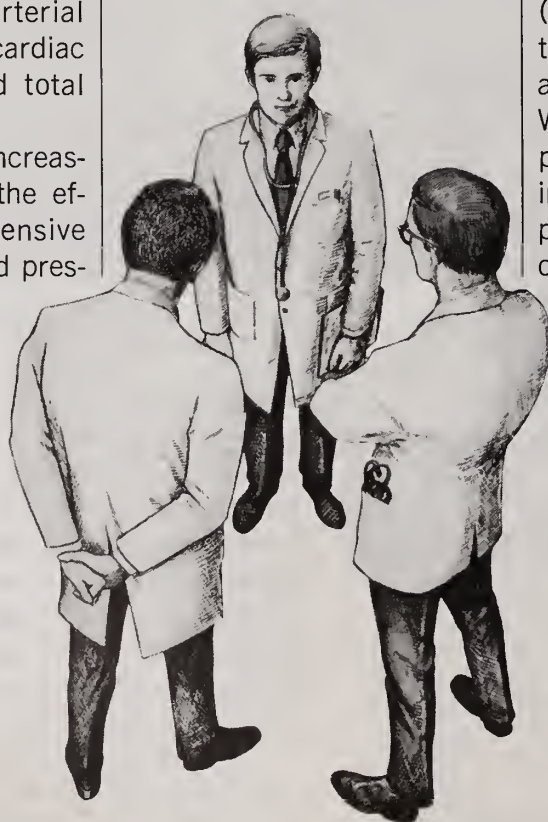
And so, physicians are increasingly concerned with the effects of an antihypertensive agent not only on blood pres-

sure itself but also on the hemodynamic pattern—in short, with the total effect of the drug. *Does it indeed help lower blood pressure effectively? Is peripheral resistance reduced? Are cardiac output and renal functions main-*

tained? And, also, is there likely to be drug-induced postural hypotension serious enough to pose a threat to the patient's cerebrovascular status?

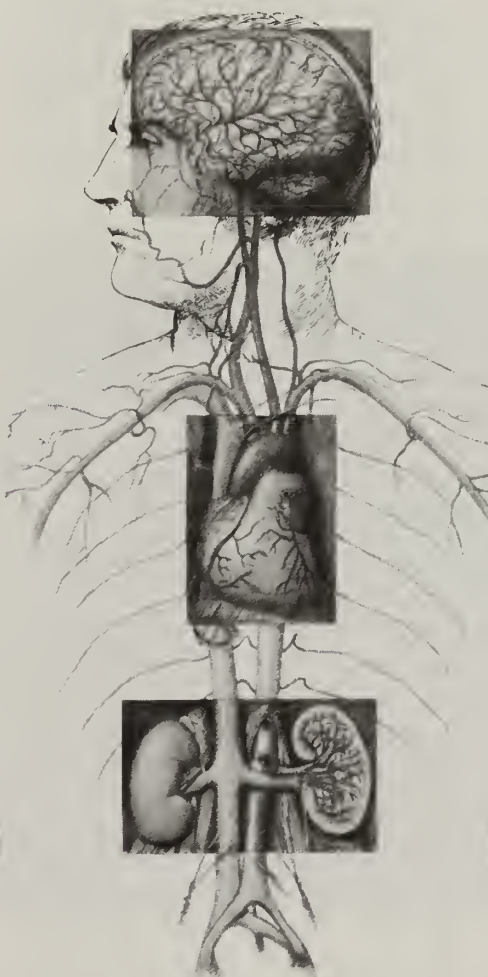
With this emphasis on overall drug performance has come a growing reliance on ALDOMET® (Methyldopa, MSD) in the treatment of sustained moderate hypertension.

With its unique hemodynamic profile, ALDOMET has drawn increasing attention and approval from physicians. First, of course, for its efficacy in



the more physicians rely on this unique antihypertensive

lowering blood pressure. But there are other considerations as well. Cardiac output is usually maintained with no cardiac acceleration; in some patients the heart rate is actually slowed. Peripheral resistance is apparently reduced. ALDOMET does not usually compromise existing renal function; it generally does not reduce renal blood flow, glomerular filtration rate, or filtration fraction. And ALDOMET usually does not cause symptomatic postural or exercise hypotension.



Contraindications include active hepatic disease and known sensitivity to the drug. Use with caution in patients with a history of liver disease or dysfunction. Not recommended in pheochromocytoma or pregnancy.

It is important to recognize that a positive Coombs test, hemolytic anemia, and liver disorders may occur with methyldopa therapy. The rare occurrences of hemolytic anemia or liver disorders could lead to potentially fatal complications unless properly recognized and managed. For more details see the brief summary of prescribing information.

In most cases of sustained moderate hypertension

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smoothly lowers blood pressure

For a brief summary of prescribing information, please see following page.

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now available in
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as well as the standard
250-mg tablets

In most cases of
sustained moderate hypertension
ALDOMET[®]
(METHYLDOPA MSD)
smoothly lowers blood pressure

Contraindications: Active hepatic disease, such as acute hepatitis and active cirrhosis. Known sensitivity. Not recommended in pheochromocytoma. Unsuitable in mild or labile hypertension responsive to mild sedation or thiazide therapy. Use cautiously in patients with history of previous liver disease or dysfunction.

Warnings: It is important to recognize that a positive Coombs test, hemolytic anemia, and liver disorders may occur with methyldopa therapy. The rare occurrences of hemolytic anemia or liver disorders could lead to potentially fatal complications unless properly recognized and managed. Read this section carefully to understand these reactions.

With prolonged methyldopa therapy, 10% to 20% of patients develop a positive direct Coombs test, usually between six and twelve months of therapy. Lowest incidence is at daily dosage of 1 g or less. This on rare occasions may be associated with hemolytic anemia, which could lead to potentially fatal complications. One cannot predict which patients with a positive direct Coombs test may develop hemolytic anemia. Prior existence or development of a positive direct Coombs test is not in itself a contraindication to use of methyldopa. If a positive Coombs test develops during methyldopa therapy, determine whether hemolytic anemia exists and whether the positive Coombs test may be a problem. For example, in addition to a positive direct Coombs test there is less often a positive indirect Coombs test which may interfere with cross matching of blood.

At the start of methyldopa therapy, it is desirable to do a blood count (hematocrit, hemoglobin, or red cell count) for a baseline or to establish whether there is anemia. Periodic blood counts should be done during therapy to detect hemolytic anemia. It may be useful to do a direct Coombs test before therapy and at six and twelve months after the start of therapy. If Coombs-positive hemolytic anemia occurs, the cause may be methyldopa and the drug should be discontinued. Usually the anemia remits promptly. If not, corticosteroids may be given and other causes of anemia should be considered. If the hemolytic anemia is related to methyldopa, the drug should not be reinstituted. When methyldopa causes Coombs positivity alone or with hemolytic anemia, the red cell is usually coated with gamma globulin of the IgG (gamma G) class only. The positive Coombs test may not revert to normal until weeks to months after methyldopa is stopped.

Should the need for transfusion arise in a patient receiving methyldopa, both a direct and an indirect Coombs test should be performed on his blood. In the absence of hemolytic anemia, usually only the direct Coombs test will be positive. A positive direct Coombs test alone will not interfere with typing or cross matching. If the indirect Coombs test is also positive, problems may arise in the major cross match and the assistance of a hematologist or transfusion expert will be needed.

Fever has occurred within first three weeks of therapy, sometimes with eosinophilia or abnormalities in liver function tests, such as serum alkaline phosphatase, serum transaminases (SGOT, SGPT), bilirubin, cephalin cholesterol flocculation, prothrombin time, and bromsulphalein retention. Jaundice, with or without fever, may occur, with onset usually in the first two to three months of therapy. Rarely fatal hepatic necrosis has been reported. These hepatic changes may represent hypersensitivity reactions; periodic determination of hepatic function should be done particularly during the first six to twelve weeks of therapy or

whenever an unexplained fever occurs. If fever, abnormalities in liver function tests, or jaundice appear, stop therapy with methyldopa. If caused by methyldopa, the temperature and abnormalities in liver function characteristically have reverted to normal when the drug was discontinued. Methyldopa should not be reinstituted in such patients.

Rarely, reversible reduction in leukocyte count with primary effect on granulocytes has been seen. Reversible thrombocytopenia has occurred rarely. When used with other antihypertensive drugs, potentiation of antihypertensive effect may occur.

Use in Pregnancy and Childbearing Age—Not recommended in pregnancy. In women of childbearing age, weigh potential benefits against possible fetal hazards.

Precautions: Methyldopa may interfere with measurement of: uric acid by the phosphotungstate method, creatinine by the alkaline picrate method, and SGOT by colorimetric methods. Since methyldopa causes fluorescence in urine samples at the same wavelengths as catecholamines, spuriously high levels of urinary catecholamines may be reported. This will interfere with the diagnosis of pheochromocytoma. Stop drug if involuntary choreoathetotic movements occur in patients with severe bilateral cerebrovascular disease. Patients may require reduced doses of anesthetics; hypotension occurring during anesthesia usually can be controlled with vasopressors. Hypertension has occurred after dialysis in patients on methyldopa because the drug is removed by this procedure.

Adverse Reactions: Sedation, usually transient, may be seen during initial therapy or when dosage is increased. Headache, asthenia, or weakness may be noted as early, transient symptoms. Symptoms associated with effective lowering of blood pressure are occasionally seen and include dizziness, lightheadedness, and symptoms of cerebrovascular insufficiency. Angina pectoris may be aggravated. Symptoms of orthostatic hypotension may occur; if symptoms occur, reduction of dosage is suggested. Bradycardia, nasal stuffiness, mild dryness of mouth, and gastrointestinal symptoms including distention, constipation, flatus, and diarrhea occur occasionally; these generally can be relieved by reducing dosage. Nausea and vomiting have been reported in only a few patients. Sore tongue or "black tongue," pancreatitis, and inflammation of salivary glands may occur.

Weight gain and edema occur infrequently and are relieved by administering a thiazide diuretic; if edema progresses or signs of pulmonary congestion appear, discontinue drug. A rise in BUN has been observed. Other rare reactions include breast enlargement, lactation, impotence, decreased libido, skin rash, mild arthralgia, myalgia, paresthesias, Bell's palsy, parkinsonism, psychic disturbances including nightmares, reversible mild psychoses or depression. Urine exposed to air after voiding may darken because of breakdown of methyldopa or its metabolites.

Note: Dosage should be limited initially to 500 mg daily when following previous antihypertensive agents other than thiazides. Maximal recommended daily dose is 3.0 g. Patients with impaired renal function may respond to smaller doses than patients with normal kidney function. Syncope in older patients has been related to increased sensitivity in those with advanced arteriosclerotic vascular disease; this may be avoided by lower doses. Tolerance occasionally seen either early or late, but more likely between second and third month after initiation of therapy; increased dosage or combined therapy with a thiazide frequently restores effective control.

How Supplied: Tablets, containing 250 mg methyldopa each, in single-unit packages of 100 and bottles of 100 and 1000; Tablets, containing 500 mg methyldopa each, in single-unit packages of 100 and bottles of 100.

For more detailed information, consult your MSD representative or see full prescribing information. Merck Sharp & Dohme, Division of Merck & Co., Inc., West Point, Pa. 19486

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ECG PROBLEMS

HISTORY: A 48-year-old man referred for evaluation because of borderline cardiac enlargement on routine chest X ray. No symptoms referable to the cardiovascular system. Blood pressure 135/85. No cardiac abnormalities except for a soft, early systolic murmur along the left sternal border.

(for diagnosis see page 581)



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BOOK REVIEWS

Allergy Management in Clinical Practice. LOUIS TUFT, M.D. Price, \$29.75. Pp. 426. St. Louis, Missouri: The C. V. Mosby Co., 1973.

In the preface of this book, Dr. Tuft tells us that the book aims to present, in as clear a manner as possible, the management of an allergy patient from the first visit and throughout the treatment period. Dr. Tuft has been in practice almost half a century and is a pioneer in the specialty of allergy. I feel he has succeeded both in presenting his approach to common clinical problems as well as reviewing the experience of others in the field.

During the last 15 years, many advances have been made in the immunology of clinical allergy. These advances have led to an understanding of the allergic reaction, the antibodies involved, the chemical mediators involved and the pharmacology of the therapeutic agents used. In vitro techniques are available or are being developed for evaluation of immunotherapy, drug allergy, basic mechanisms in asthma. Dr. Tuft touches on these in his introductory chapters and, though the information is incomplete, he obviously has kept up in this rapidly changing field.

I found the chapters on Diagnosis and Treatment excellent. When a patient presents to an allergist for evaluation the following questions need answers: Is the condition allergic? If so, what is the cause? History, physical examination, laboratory tests, allergy skin testing if indicated all lead to the diagnosis. It is important to realize here that not all patients presenting to the allergist have an allergic condition and that not all those who have an allergic condition require skin testing (e.g. urticaria, atopic dermatitis). Not all patients with respiratory allergy who have positive skin tests require immunotherapy. If avoidance of the offending allergen or symptomatic therapy will result in symptomatic control, that is all that needs to be done.

The main body of the book contains chapters on serum allergy, drug reactions, food allergy, insect allergy and respiratory allergy. There are also chapters on urticaria, atopic dermatitis, ocular allergy, contact dermatitis and miscellaneous allergic conditions. Both the author's experience and that of others is presented. When the author's method of therapy is one that is not accepted by all allergists (such as use of alum-precipitated, pyridine extracts, Allpyral, Dome Lab, in immunotherapy), he notes that fact and presents both viewpoints.

In reading over the book, I did not agree with his classification of atopic versus non-atopic serum

allergy or drug reactions. I feel the mechanisms are the same but that one occurs in an atopic person (i.e. a person with a history of hay fever or asthma). Recent surveys do not indicate that an atopic person is more likely to develop a drug reaction than a non-atopic person. Dr. Tuft advocates early use of steroids in asthma because he feels it will help more early than too late. Most of us would use steroids in asthma only when other measures have failed to control the attack.

Dr. Tuft's book can be highly recommended for the pediatrician, internist, general practitioner, and otolaryngologist who see patients with allergic conditions.

ISAAC WEISZER, M.D.

The Newborn Chest. L. WESENBERG, M.D. Price, \$20.00. Pp. 296. Hagerstown, Maryland: Harper & Row, 1973.

With the growing importance of neonatology, there exists a need for a definitive text on interpretations of X-rays of the newborn chest. This monograph is a good first step towards that goal. The text is separated into four main sections including one on the normal chest, a second on the medical conditions of the chest, a third on the surgical conditions of the chest, and finally a section on congenital heart disease. Each section is followed by an extensive, pertinent, and up-to-date bibliography. The reproductions of the radiographs are good throughout, however the legends under them and their relationship to the text are often difficult to follow.

The first section concerns the interpretation of the normal newborn chest and is of importance for the pediatrician and pediatric surgeon as a good teaching guide for learning to interpret newborn chest roentgenograms.

The section on medical conditions of the newborn chest has many good and interesting chapters. Occasionally the author presents his personal hypothesis as a proven fact and the non-radiologist may be unable to ferret out the theories from the facts. This is especially pertinent in Chapter Four on Wet-Lung Disease, where there are at least two different schools of thought as to the etiology and only one is presented.

The section on surgical conditions of the newborn chest contains some admirable and distinctive X-rays, but also contains medical inaccuracies and differential diagnoses that are incomplete. The radiologic

BOOK REVIEWS

approach to the individual patient is described but a clinician would have difficulty understanding how to approach the *patient* who has a suspected surgical condition in the chest. The pathophysiology and classifications are insufficient for the surgeon and are occasionally misleading.

The author has chosen to discuss congenital heart disease in a separate fourth section instead of including these diseases among the medical and surgical conditions from which the clinician must differentiate them. The failure to discuss the difficulty and methods of separating out congenital

heart disease from medical and surgical problems in the newborn is the one major weakness of this book.

In conclusion, this monograph presents an extensive and up-to-date bibliography that would be of great help to any physician wishing to learn more about interpretation of the newborn chest. The pediatric surgeon, neonatologist, and pediatrician will find this a handy guide for specific problems in interpretation of the newborn chest and radiologists should own this book.

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THE VIEW BOX

(from page 542)

DIAGNOSIS: CALCIFIED SUBDURAL HEMATOMA

The location and the character of the calcification in this case is rather typical. Subdural hematomas most often occur over the convexity of the parietal lobe; can extend into the temporal fossa and into the interlobar fissure. In about 20% the lesion is bilateral.

It takes at least several months and probably years for subdural hematomas to calcify and the improved health care makes the calcified subdural hematoma an unusual finding in a plain skull x-ray.

*Edited by Gunter J. Augustin, M.D.
Senior Attending Radiologist, Washington
Hospital Center, Washington, D.C.*

ECG PROBLEMS

(from page 575)

INTERPRETATION: 1. Probable left ventricular hypertrophy.

Initially, this tracing looks essentially normal despite the large QRS amplitude. This single feature can be discounted in a young adult, particularly with a slender build such as this patient had. However, there also is prolongation of the ventricular activation time. This is clearly seen in lead V_6 where the peak of the R wave is reached at least .05 seconds after the beginning of the QRS complex. With the Estes criteria for left ventricular hypertrophy, this observation satisfies one point. Three points are given for QRS complexes which exceed 25 mm. of either R wave or S wave in the chest leads. This gives a total of four points which is enough to diagnose probable left ventricular hypertrophy. Depending upon where the measurements are made in the limb leads, the QRS duration may be .08 or .09 seconds. If .09 seconds or more is the duration of the QRS complex, that would be worth one more point, adding up to a total of five which would then be diagnostic of left ventricular hypertrophy.

This case is particularly interesting in that the patient does not have heart disease. He is a marathon runner, having won a 26 mile race only a few months before this electrocardiogram was taken. He averages running 30-40 miles per week even when he is not in strenuous training. His left ventricular "hypertrophy" probably really represents simply a thick, muscular left ventricular wall. The fact that this is simply a physiologic response without disease may explain why there are no ST or T wave changes in the left precordial leads as one finds with the usual left ventricular hypertrophy induced by heart disease.

*Edited by
Robert R. Montgomery, M.D.*



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The entire manuscript, including footnotes and case reports, should be submitted unrolled, with double type spacing. An original copy and one carbon copy should be submitted, and a carbon copy should be retained by the author.

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References should be double spaced, on a separate sheet, and listed in order of citation in the text. Superior numbers should be inserted in the text at points of citation.

References should be given in the style regularly used in THE ANNALS, eg:

Seremetis, M.D., DeGuzman, V.C.,
Lyons, W.S., Peabody, J.W.: Complications of Cardiac Pacemakers, Medical Annals of D.C., 1973, 42, 165.

TEXT

Use generic or descriptive names of drugs when available. Trade names, capitalized, may be given in parentheses when the drug is first mentioned.

Statistics should be checked for consistency within the text and for agreement with graphs or tables.

Laboratory data should not be given in abbreviated form but in full (e.g., "hemoglobin level, 12 Gm. per 100 ml." rather than "Hb. 12 GM.%).

Figures should be used for number 10 and above, laboratory measurements, percentages, and ages.

Metric equivalents should be given for dosage and body height and weight.

Centigrade equivalents should be given for Fahrenheit body temperatures, and vice versa.

Abbreviations should be used sparingly, with expansion given for those not listed in standard medical dictionaries.

The meaning of "we" should be clarified, especially if there is only one author. Avoid use of editorial "we."

SUBHEADINGS

One center heading should be supplied for about every three pages of double-spaced text copy. Subdivisions of main topics should be indicated by side headings.

SUMMARY

The summary should be brief, giving specific facts concerning the study and its results.

ADDRESS

The street address of one author should be given at the end of the article for reprint requests and correspondence.

TABLES

The title should be given at top of the page for each table.

Approximate placing of tables in text should be indicated, and each table should be referred to in the text.

The meaning of abbreviations should be clear, with those not listed in standard medical dictionaries expanded in a footnote to the table.

There should be no discrepancies in the totals.

Figures should be consistent with the text, without extensive duplication between tables and text or graphs.

All material under each column heading should be parallel in meaning.

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Simple tabular material should be incorporated into the text in sentence form.

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Photographs should be submitted as unmounted black-and-white glossy prints.

Graphs and line drawings should be prepared with black india ink on white paper, with uniform lettering which will be legible when the illustration is reduced to 3-1/8-in. in width.

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The top of each illustration should be indicated.

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Dorsey Laboratories 5, 11

Eli Lilly & Company 12

McNeil Laboratories T-567

Merck, Sharp & Dohme Laboratories .. T-572-574

Pharmaceutical Manufacturers

Association T-564-565

Reed & Carnrick T-566

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Roche Laboratories C2, 1, C3, C4

G. D. Searle & Company T-558-559

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Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, espe-

cially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests

advisable during protracted therapy.

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Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive dis-

orders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anti-convulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful

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According to her major symptoms, she is a psychoneurotic patient with severe anxiety. But according to the description she gives of her feelings, part of the problem may sound like depression. This is because her problem, although primarily one of excessive anxiety, is often accompanied by depressive symptomatology. Valium (diazepam) can provide relief for both—as the excessive anxiety is relieved, the depressive symptoms associated with it are also often relieved.

There are other advantages in using Valium for the management of psychoneurotic anxiety with secondary depressive symptoms: the psychotherapeutic effect of Valium is pronounced and rapid. This means that improvement is usually apparent in the patient within a few days rather than in a week or

two, although it may take longer in some patients. In addition, Valium (diazepam) is generally well tolerated; as with most CNS-acting agents, caution patients against hazardous occupations requiring complete mental alertness.

Also, because the psychoneurotic patient's symptoms are often intensified at bedtime, Valium can offer an additional benefit. An *h.s.* dose added to the *b.i.d.* or *t.i.d.* treatment regimen can relieve the excessive anxiety and associated depressive symptoms and thus encourage a more restful night's sleep.

For further information on this subject, the following references are provided:

1. Henry BW, *et al*: *Dis Nerv Syst* 30:675-679, Oct 1969.
2. Hollister LE, *et al*: *Arch Gen Psychiatry* 24:273-278, Mar 1971.
3. Claghorn J: *Psychosomatics* 11:438-441, Sept-Oct 1970.

surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of child-bearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies.

Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle

spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.



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CONTENTS

SCIENTIFIC ARTICLES

- Treatment of Parkinson's Disease with Carbidopa, A Peripheral Decarboxylase Inhibitor and Levodopa.** Joseph Ferganlich, M.D. 587
- Transient Global Amnesia.** Harold Stevens, Ph.D., M.D., and Bruce J. Ammerman, M.D. 593
- Selective Hypoaldosteronism: A Case Report and Review of Literature.** Iluminado A. Cruz, M.D., Martin G. Dillard, M.D., and Adrian O. Hosten, M.D. 597

SPECIAL ARTICLE

- Public Behavior During an Air Pollution Episode: Implications for Health Planning.** Melba Price, B. A. and Bailus Walker, Jr., M.S.P.H. 603

OTHER FEATURES

- Editorial** 5
 To The Editor. Tzu-Min Kao, M.D., Cheng-Nan Chen, M.D., Fred Chin Chu, M.D.
- Post Graduate Education** 9
 Treatment of Malabsorption Syndromes. Francis Horrigan, M.D.
 The Systolic Click—Late Systolic Murmur Syndrome. James A. Ronan, Jr., M.D.
- Index to Volume XLII (1973)** 615
 Medical Annals of the District of Columbia
- Index to Volume XLIII (1974)** 623
 Medical Annals of the District of Columbia
- ECG Problems** 592
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Editorial

To the Editor

As physicians, whose ancestry is Chinese, we would like to address the practice of acupuncture. One of us (TMK) has been an active student and teacher of both "western" and "Chinese" medicine for the past 16 years.

First of all, it is necessary to state that universally the goal of medicine is to help patients recover from their illnesses. At the same time, it is the responsibility of the physician to do no harm while administering his aid. These general principles are taught in and apply equally to both "western" and "Chinese" medicine.

As an aside, we must insist that the distinctions between medicine practiced in the West and in China are artificial and temporary due to cultural isolation. With a meaningful exchange of knowledge, one could hope that eventually the best therapeutic resources of either system will be available to every patient.

With specific regard to acupuncture, we hope that an openness of mind can be maintained. After all, what is the essence of acupuncture? It is not a miraculous cure-all; it is not black magic. It is, however, a set of medical maneuvers (undoubtedly foreign to the non-Oriental) that through the years have helped many patients with a variety of conditions.

The question today no longer is "Will it work?" but "How and where can acupuncture be used to the benefit of the patient?"^{1,2} Like any procedure newly introduced to the medical community, there must be understanding and due caution exercised in its application. If practiced *with care*, its relative lack of side-effects and its therapeutic effectiveness may make acupuncture the treatment of choice in selected clinical situations, especially as an anesthetic or in the treatment of pain.

Secondly, since acupuncture is a healing art, the person who practices it must have some basic medical training in addition to his skill in inserting acupuncture needles into the body³. There are a number of published reports of needles accidentally inserted into the lungs^{4,5}, the kidneys⁶, the heart⁷ and many warnings in Chinese text-books about inserting needles carelessly around the eyes⁸. A number of acupuncture points, in fact, are "forbidden for use"⁹ because of their proximity to anatomical structures, which, if punctured, would mean danger to the patient. A basic knowledge of anatomy, therefore, is prerequisite to the practice of acupuncture.

At the same time, the person recommending acupuncture therapeutically must have a sound idea

of its uses in specific diseases. Acupuncture is not good for everything and should only be recommended conservatively, when appropriate.

In Washington, D.C. there may be the greatest number of unlicensed acupuncturists in America. At present, they practice under a physician's supervision—with the regulations being interpreted rather loosely. Meanwhile, there is no way to verify the credentials of any person representing himself to be an acupuncturist. In fact, for a fee, diplomas can be purchased in the Far East that certify the study of acupuncture¹⁰. Without adequate qualifications and without adequate supervision, untrained or poorly trained acupuncturists are surely a menace to the public health of the community.

Finally; there have been many exaggerated statements¹¹ and misleading advertisements about the uses of acupuncture as a therapeutic procedure. An unsuspecting patient can erroneously build up his expectations without the benefit of unbiased advice. A culmination of such disappointments¹² may prompt public judgment to unnecessarily limit the practice of acupuncture altogether. In effect, "the baby would have been tossed out with the wash-water."

Given the present situation, in which large numbers of patients are apparently receiving acupuncture on the basis of faith alone, without understanding fully the indications for the technique, and in which the acupuncturists are of uncertain and unverifiable qualifications, we feel that a more conservative approach to the practice of acupuncture should be considered in Washington, D.C.

Our specific recommendations are the following:

- 1) As the practice of acupuncture is in fact the practice of medicine, for the present it is necessary to *restrict* the use of acupuncture to licensed physicians (and perhaps dentists). The patient would at least have the assurance that his acupuncturist did at one time study and pass some basic medical courses.
- 2) If it is then found necessary to have non-physician acupuncturists administer the needles, then a paramedical examination should be developed which would include some basic understanding of anatomy, the general principles of medicine and a knowledge of acupuncture.
- 3) Advertising and other forms of spectacular and unsubstantiated claims of success must be prohibited. The air of sensationalism surrounding acupuncture must be eliminated to insure the accurate and effective use of acupuncture. Acupuncture is a medical procedure whose

applications must be considered soberly.

It is our hope that acupuncture can find its place in medicine as practiced in Washington, D.C. Its use must be controlled for the present by a physician who can prudently affirm its use for a given situation. Otherwise, given a few "honest" mistakes by untrained acupuncturists and there will be no acupuncture for anyone, not even those who might benefit from its use.

Very truly yours,

Tzu-Min Kao, M.D.

Cheng-Nan Chen, M.D.

Fred Chin Chu, M.D.

References

1. RESTON, J.: A view from Shanghai, *NY Times*, August 22, 1971, Section 4, page 13, columns 1, 2.
2. DIMOND, E. C.: Acupuncture anesthesia: western medicine and Chinese traditional medicine. *JAMA*, 1971, 218:1558-1563.
3. VEITH, I.: *The Yellow Emperor's Classic of Internal Medicine*. Berkeley, University of California Press, 1972.
4. GOLDBERG, I.: Pneumothorax associated with acupuncture. *Med J Aust*, May 12, 1973, pages:941-942.
5. CORRETT M., SINCLAIR M.: Acu- and pleuro-puncture. *NEJM*, 1974, 290:167-168.
6. KELLER, W. J., PARKER S. G., GARVIN J. P.: Possible renal complications of acupuncture. *JAMA*, 1973, 222:1559.
7. SCHIFF A. F.: A fatality due to acupuncture. *Med Times (Lond)*, 1965, 93:630.
8. (e.g. Ching-ming point, located in the medial canthus) *Acupuncture*. Ed. by Hupei province Department of Health. Peking, People's Health Publishers, 1970.
9. (e.g. Jen-ying point, located near the common carotid artery in the neck or the Chueh-pen point, located over the apex of the lung.) Chu, L.: *Modern acupuncture and moxibustion*. Hong Kong, Shao Hua Cultural Service, 1954.
10. Editorial: Shortcuts to acupuncture knowledge. *Acupuncture Research*, 1974, 2:4-5.
11. ROSENFELD, M.: DC needle therapy is assailed. *Washington Post*, May 31, 1974, Section C, page 1.
12. CARRON, H., EPSTEIN, B. S., GRAND, B.: Complications of acupuncture. *JAMA*, 1974, 228:1552-1554.

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arrhythmias. In children, overdose may cause vomiting, cardiac arrhythmias, and severe agitation. Ephedrine should be used with caution in the presence of severe cardiac disease, particularly arrhythmias and angina pectoris; avoid in hyperthyroidism and severe hypertension. Phenobarbital may be habit-forming. Avoid overdose. Potassium Iodide: Discontinue in the presence of skin rash, swelling of the eyelids and severe frontal headache. Long use may cause goiter. **ADVERSE REACTIONS:** Aminophylline/Theophylline may cause nausea, cardiac arrhythmias, and aggravate severe myocardial disease. It may cause headaches and tachycardia. Vomiting and dizziness are not uncommon. Ephedrine: In patients hypersensitive to CNS stimulation, ephedrine may cause nervousness, tachycardia, extrasystole and ventricular arrhythmias. May cause urinary retention, especially in the presence of partial prostatic obstruction. Psychoneurosis may be aggravated. Pre-existing anginal pain will be aggravated. Phenobarbital may produce severe skin rash. Avoid overdose. May be habit-forming. Potassium Iodide may cause nausea. Over very long period of use, iodides cause goiter. Discontinue if patient develops skin rash, eye irritation, eyelid swelling, or severe frontal headache.

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POST GRADUATE EDUCATION

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Once the etiology and extent of the malabsorption is established, return of normal nutrition may be obtained by the use of dietary control, antibiotics, steroids, replacement of malabsorbed nutrients, surgery or combinations of these. Representative types of malabsorption will be discussed, not because of frequency, but to demonstrate the spectrum of mechanisms and therapeutic maneuvers which may be obtained.

The post gastrectomy state represents a spectrum of malabsorption ranging from simple iron or B12 deficiency to flagrant malabsorption of fats, proteins, and other nutrients and may be multifactorial in origin. Food may undergo inadequate mixing in the stomach with rapid emptying and transit in the gut; there may be failure of pancreatic or biliary secretion due to inadequate stimulation of the duodenal mucosa or failure of these secretions to "catch up with" foods; there may be bacterial overgrowth in a blind loop producing inadequate micellar formation because of deconjugation or dehydroxylation, competition for nutrients, or bile salt diarrhea. Rational therapy may then call for simple replacement, for example of B12, or regulation of eating habit (e.g. several small meals/day), a trial of a broad spectrum antibiotic such as tetracycline 250 mg. qid for 10-14 days to alter bacterial flora or, in extreme cases, revision of the gastroenterostomy to delay gastric emptying and permit greater contact of food with pancreatic-biliary secretions.

Pancreatic insufficiency is most commonly seen in chronic pancreatitis, in the post-pancreatectomized patient, and occasionally in pancreatic carcinoma and in the increasing numbers of adult cystic fibrosis patients. Absorption can be improved in these patients by the use of pancreatic enzyme supplements. Cotazyme or viokase are effective preparations. Large doses are required (8-12 caps/day) which may be administered in divided doses just before meals or hourly throughout the day. Occasionally, sodium bicarbonate given before meals may be required to enhance the effect of the enzymes. Adequate control of the frequently coexistent diabetes will improve nutrition as will cessation of alcohol abuse.

Celiac disease is a fairly common form of malabsorption in which the absorptive surface of the small bowel mucosa becomes shortened and ineffective because of loss of brush border enzymes and dedifferentiation of the absorptive columnar epithelium of the villus, probably due to an immunologic reaction to gluten metabolites. Documentation of the mucosal damage on a normal diet and its remission with treatment provide the rationale for therapy in this disease—the strict gluten free diet. This diet must be followed for life. It is not uncommon for the celiac patient to be asymptomatic during adolescence and early adulthood; however, the temptation to relax dietary restriction must be resisted, not only to maintain optimal nutrition but also in hope of avoiding the long term risk of malignancy to which celiacs are prone, particularly to bowel lymphoma or carcinoma of the small bowel or esophagus. The severely ill patient with untreated sprue may require replacement therapy acutely (for example, 1-2 Gm calcium gluconate IV or 0.5-1 Gm magnesium sulfate in 200-500 ml. slowly IV for tetany, parenteral administration of 10-25 mg. vitamin K for the severely hypoprothrombinemic patient, or, in severe cases, parenteral hyperalimentation. Corticosteroids, in short courses, may be useful to ameliorate the secondary adrenal insufficiency occasionally seen in these patients and to stabilize mucosal lysosome hydrolase activities until the beneficial effects of the diet have restored adequate nutrition.

Regional enteritis is a common idiopathic inflammatory bowel disease which in extensive cases can produce a malabsorption of nutrients by different mechanisms—inflammatory destruction of the mucous membrane, lymphatic obstruction, decreased bile salt pool due to extensive ileal malabsorption, short circuiting of uninvolved bowel by fistulization, for example. Specific etiologic therapy aimed at Crohn's disease is lacking. However, some patients can achieve a clinical remission with prednisone 30-40 mg. per day. Data on the efficacy of azulfidine therapy in this condition are lacking but some patients seem to respond to doses of 4-8 Gm per day with follow up monitoring for the hematologic and systemic complications of the drug. Replacement therapy with iron, folic acid, B12, vitamin K and so on may become indicated, depending on the type of involvement of the bowel mucosa. Surgery may become necessary in selected cases to correct fistulas or obstruction.

Malabsorption may also occur in systemic disease which affect the bowel incidentally. Examples of this

POST GRADUATE EDUCATION

phenomenon include diabetes mellitus and scleroderma. Brittle, insulin-requiring diabetes may affect the GI tract, usually in association with evidence of neuropathy elsewhere. Gastric and intestinal hypomotility may contribute to diarrhea or constipation, occasionally with steatorrhea. Pancreatic secretions may be suboptimal due to submaximal stimulation from delayed gastric emptying; however, replacement therapy with pancreatic enzymes is usually ineffective. Bacterial overgrowth due to stasis is occasionally a factor and therapy with tetracycline 1-2 Gm. per day for 2 weeks may be beneficial in up to a third of cases. Achieving optimal diabetic management will not reverse the neuropathy but may improve gastric emptying by control of blood sugar.

Scleroderma commonly involves the GI tract, most commonly the esophagus. The small intestine is the second most frequent site of involvement and is characterized by fibrosis of the submucosal and muscle layers resulting in decreased motility, stasis and bacterial overgrowth. Broad spectrum antibiotics can at least partially eliminate the resulting moderate malabsorption.

Therapy of malabsorption syndromes therefore depends on the establishment of an etiologic diagnosis, proper replacement of nutritional deficiencies, and careful treatment directed toward the etiology as well as long term monitoring of the effects of such therapy.

Francis Horrigan, M.D.

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THE SYSTOLIC CLICK—LATE SYSTOLIC MURMUR SYNDROME

James A. Ronan, Jr., M.D.
Associate Professor
of Medicine
Georgetown University
Medical Center

Systolic clicks and late apical systolic murmurs are common cardiac auscultatory findings which have been described in as high as 0.33 percent of young female students.¹ There is ample evidence, by angiography,^{2,3} intracardiac phonocardiography,^{4,5} and echocardiography^{6,7} that these events originate in the mitral valve. The spectrum of auscultatory findings includes the isolated systolic click, the click accompanied by the late systolic murmur, and the late systolic murmur alone. (See Fig. 1)

The findings are predominantly seen in young women, but may occur in either sex from infancy to old age. Chest pain, cardiac arrhythmias and electrocardiographic changes of "ischemia" occur so frequently with the auscultatory features that they have been identified as a syndrome: the systolic click-late systolic murmur syndrome, or the billowing mitral valve syndrome.^{8,9,10}

The chest pain is usually of a musculoskeletal type but occasionally is similar to angina pectoris. Coronary arteriograms have not shown intraluminal arterial narrowing.¹¹ It has been postulated that the pain is caused by the prolapse of the mitral valve leaflet producing tension and ischemia in the papillary muscle.¹² Other symptoms which may occur are dyspnea, lightheadedness, and anxiety.

The apical systolic clicks may be single or multiple and almost always occur in mid or late systole. The heart murmur which may accompany the clicks usually begins after the first click and extends up to the second heart sound. The timing of these auscultatory events change dramatically when the pressure and volume relationships of the left ventricle are altered.^{13,14} They appear earlier when the patient is sitting, standing, after physical exercise, or

after the inhalation of amyl nitrite, and later with administration of a vasopressor, with squatting, or with isometric handgrip exercise. The intensity of the murmur responds to the vasoactive drugs like the other forms of mitral regurgitation: becoming louder with a vasopressor and fainter immediately after amyl nitrite inhalation.¹⁴ Amyl nitrite often produces a biphasic response of this late systolic murmur, so that the murmur may become even louder than in the control state at 30-60 seconds after the onset of inhalation.

The electrocardiogram may be abnormal, particularly with T wave inversions in Lead II, III, and aVf. Q waves in the inferior leads and left axis deviation occasionally occur. Premature ventricular beats are quite common and premature atrial beats and paroxysmal tachycardia or fibrillation are sometimes seen.¹⁵ The electrocardiographic abnormalities are more frequent and more severe in those patients with more extensive mitral valve prolapse.

Cardiac enlargement is not usually present unless mitral regurgitation is at least of moderate degree. Chest X-ray, however, often shows a narrowed anteroposterior dimension of the chest, as well as frequent cases of mild pectus excavatum, mild thoracic scoliosis, or loss of the normal kyphotic curve of the thoracic spine, ("straight back").¹⁶

Although there is little anatomic information about the etiology of these findings, myxomatous degeneration of the valve,¹⁷ elongation of the chordae tendineae,¹⁸ and redundant valve leaflets have been described, hence the name, "the floppy valve." It has been seen in the Marfan syndrome and after rheumatic fever, but usually the etiology is

POST GRADUATE EDUCATION

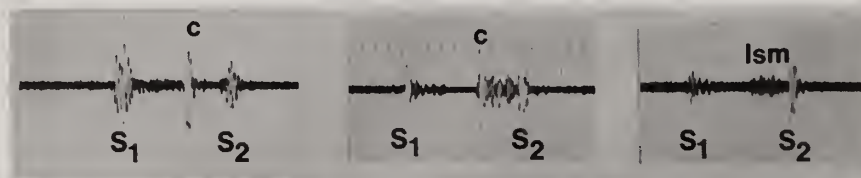


Figure 1

c = systolic click

lsm = late systolic murmur

s₁ = first heart sounds₂ = second heart sound

Left hand panel: demonstrates the phonocardiogram of a patient with isolated systolic click.

Middle panel: demonstrates the phonocardiogram of a patient with a systolic click followed by a late systolic murmur.

Right hand panel: demonstrates the phonocardiogram of a patient with isolated late systolic murmur.

unknown. There is a familial tendency to this abnormality and it has been described as an autosomal dominant trait.¹⁹

It is usually tolerated well. Since endocarditis may occur,²⁰ patients should have prophylaxis against endocarditis at the time of dental work, infected wounds, cystoscopy, general surgery, etc. Although rheumatic fever infrequently causes these findings,¹⁵ when the evidence is clear that it is rheumatic in origin, then continuous prophylaxis against beta streptococcal infection should be provided.

The ventricular arrhythmias are usually quite mild and do not require therapy. However, when patients are symptomatic due to the arrhythmia, or if ventricular tachycardia or very frequent premature ventricular contractions occur, they should be treated. Propranolol is often an effective drug in this treatment. Although sudden death has occurred, when we compare the few cases of sudden death to the large number of people affected, we recognize its rarity. Mitral regurgitation is seldom severe enough to require mitral valve surgery, but occasionally this has been done.¹² Mitral valvuloplasty, rather than mitral valve replacement, is preferred by some surgeons since there is adequate valve substance to allow the surgeon to tailor the valve and reduce regurgitation.

References

1. RIZZON, P., GIUSEPPINA, B., BRINDICCI, G., AND MAURO, F.: Familial syndrome of midsystolic click and late systolic murmur. *Brit. Heart J.* 35:245-259, 1973.
2. CRILEY, J. M., LEWIS, K. B., HUMPHRIES, J. O., ET. AL.: Prolapse of the mitral valve. Clinical and cine-angiographic findings. *Brit. Heart J.* 28:488-496, 1966.
3. JERESATY, R. M.: Ballooning of the mitral valve leaflets: angiographic study of 24 patients. *Radiology* 100:45-52, 1971.
4. RONAN, J. A., PERLOFF, J. K., HARVEY, W. P.: Systolic click and the late systolic murmur. Intracardiac phonocardiographic evidence of their mitral valve origin. *Am. Heart J.* 70:319-325, 1965.
5. LEON, D. F., LEONARD, J. J., AND KROETZ, F. W.: Late systolic murmurs, clicks, and whoops arising from the mitral valve. *Am. Heart J.* 72:325, 1966.
6. SHAH, P. M., AND GRAMIAK, P.: Echocardiographic recognition of mitral valve prolapse (Abstr.) *Circulation* 42:III-45, 1970.
7. POPP, R. L., BROWN, O. R., SILVERMAN, J. F., AND HARRISON, D. C.: Echocardiographic abnormalities in the mitral valve prolapse syndrome. *Circulation* 49:428-433, 1974.
8. BARLOW, J. B., BOSMAN, C. K., POCOCK, W. A., AND MARCHAND, P.: Late systolic murmurs and non-ejection ("mid late") systolic clicks: an analysis of 90 patients. *Brit. Heart J.* 30:203-218, 1968.
9. BARLOW, J. B., BOSMAN, C. K.: Aneurysmal protrusion of the posterior leaflet of the mitral valve: An auscultatory-electrocardiographic syndrome. *Am. Heart J.* 71:166-178, 1966.
10. HANCOCK, E. W., AND COHN, K.: The syndrome associated with midsystolic click and late systolic murmur. *Amer. J. of Med.* 41:183-196, 1966.
11. LOBSTEIN, H. P., HORWITZ, L. D., CURRY, G. C., AND MULLINS, C. B.: Electrocardiographic abnormalities and coronary arteriograms in the mitral click-murmur syndrome. *N E J M* 289:127-131, 1973.
12. JERESATY, R. M.: Mitral valve prolapse-click syndrome. *Prog. in Cardiovasc. Dis.* 15:623-652, 1973.
13. FONTANA, M. E., PENCE, H. L., LEIGHTON, R. F., WOOLEY, C. F.: A postural auscultatory phenomenon. *Circulation* 41:807-816, 1970.
14. BARLOW, J. B.: Conjoint clinic on the clinical significance of late systolic murmurs and non-ejection systolic clicks. *J. Chron. Dis.* 18:665-673, 1965.
15. POCOCK, W. A., AND BARLOW, J. B.: Etiology and electrocardiographic features of the billowing posterior mitral leaflet syndrome: Analysis of a further 130

-
- patients with a late systolic murmur or nonejection systolic click. *Amer. J. of Med.* 51:731-739, 1971.
16. de LEON, A. C., JR., AND RONAN, J. A., JR.: Thoracic bony abnormalities with the click and the late apical systolic murmur (Abstr.) *Circulation* 44:Supp II, 157, 1971.
17. SHERMAN, E. B., CHAR, F., DUNGAN, W. T., ET. AL.: Myxomatous transformation of the mitral valve producing mitral insufficiency: Floppy valve syndrome. *Am. J. Dis. Child.* 119:171-575, 1970.
18. EDWARDS, J. E.: Clinicopathologic correlations: Mitral insufficiency resulting from "overshooting" of leaflets. *Circulation* 43:606-612, 1971.
19. SHELL, W. E., WALTON, J. A., CLIFFORD, M. E., AND WILLIS, P. W. III: The familial occurrence of the syndrome of mid-late systolic click and late systolic murmur. *Circulation* 39:327-337, 1969.
20. Le BAUER, E. J., PERLOFF, J. K., AND KELIHER, T. F.: The isolated systolic click with bacterial endocarditis. *Am. Heart J.* 73:534-537, 1967.



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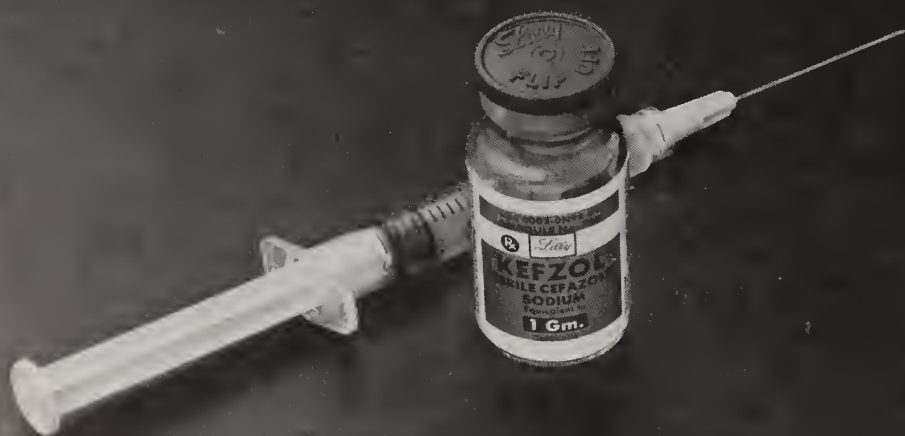
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SCIENTIFIC ARTICLES

Treatment of Parkinson's Disease with Carbidopa, A Peripheral Decarboxylase Inhibitor, and Levodopa

JOSEPH FERMAGLICH, M.D.

Abstract

The addition of carbidopa to levodopa in the treatment of Parkinson's disease resulted in a mean reduction of approximately 73% of orally administered levodopa, usually with equivalent antiparkinsonian benefit. By varying the levodopa:carbidopa ratio, suppression of gastrointestinal distress and decrements in dystonic movements may be achieved. Thus, it is concluded that carbidopa is a useful adjunct in the treatment of Parkinsonism. It does not replace levodopa, which is still the preferred treatment.

Introduction

Levodopa is the preferred treatment of Parkinson's disease.¹⁻⁴ Its usefulness, however, is limited by the large oral daily doses required, often demanding frequent administration, and the high incidence of complications of treatment. Amongst the latter are intractable gastrointestinal distress, nausea, vomiting, abnormal involuntary movements, and psychiatric disorders. Usually they are dose related and respond to a reduction of the quantities of administered levodopa.¹⁻⁷

In Georgetown University patients, the levodopa:carbidopa ratio was greater than 14:1. Yet in this group, centrally mediated complications of treatment were somewhat lower than in four other studies, and more effective antiparkinsonian control was achieved. This leads to the conclusion that the higher doses of carbidopa, or the lower doses of levodopa required to suppress intractable gastrointestinal distress, result in the potentiation of centrally mediated complications or diminished antiparkinsonian control.

Accumulating evidence indicates that most orally administered levodopa is metabolized peripherally, although the biological importance and identity of many metabolites remain unknown.⁸⁻¹⁵ Since decarboxylation is a major peripheral metabolic pathway, inhibition of extracerebral aromatic L-amino acid decarboxylase has been utilized to increase available quantities of unchanged levodopa for entry into brain where it is presumed to be converted to dopamine in surviving neurons of the nigrostriatal

tract. One decarboxylase inhibitor which does not cross the blood brain barrier at ordinary doses is carbidopa (L-alphamethyldopahydrazine) the hydrazino derivative of methyldopa.¹⁶⁻²¹

The purpose of this report is to describe experience with the use of the combination of levodopa and carbidopa in Parkinsonian patients for periods as long as one year.

Methods

Forty patients with idiopathic Parkinson's disease were treated. Twenty-one were men and nineteen were women. Ages ranged from 52-83 years, the mean being 62.37 years. Two patients (5%) were treated *de novo*, whereas 38 (95%) were crossed over from treatment with levodopa alone. The mean duration of previous treatment with levodopa alone was 36.92 months. Twenty eight patients treated with the combination had tremor, 39 were rigid, 35 demonstrated bradykinesia and 19 were dystonic. Thus, the purpose of the crossover was to attempt to improve antiparkinsonian responses and decrease dystonic movements.

TREATMENT OF PARKINSON'S DISEASE WITH CARBIDOPA

FERMAGLICH

All patients were treated on an out-patient basis. Those treated *de novo* were started on levodopa, and carbidopa was added subsequently. The doses of levodopa in crossover patients were reduced initially by approximately one third. Thereafter, carbidopa was added and the dose was increased slowly, while further reductions of levodopa were made. Neurological disability was rated according to the scale proposed by McDowell *et al*⁴. Parameters of hematopoietic, renal and hepatic function were monitored at regular intervals.

Results

On combination therapy, the range of levodopa was 0.2-3.5 grams per day, the mean being 1.05 grams per day. This contrasted with a previous range of levodopa alone in the crossover patients of 1.8-8.0 grams per day, the mean being 3.80 grams per day. The range of doses of carbidopa was 20-150 mgs per day, the mean being 73.55 mgs per day. Thus, the mean ratio of levodopa to carbidopa when on combination therapy was 1.05:0.074 (levodopa/carbidopa = 14.18:1), and the mean daily dose of levodopa was reduced by approximately 73%.

Thirty two patients (80%) have continued combination therapy. Improvements noted in their Parkinsonian symptoms and signs are listed in Table I. Tremor was decreased by 50% or more in 19 (59%) patients. In two patients (6%) tremor was aggravated. Five (16%) patients were noted to have equivalent tremor after addition of carbidopa.

Rigidity was improved by 50% or more in 25 (78%) patients. Eleven (34%) patients were noted to have equivalent rigidity after addition of carbidopa, but no patient's rigidity was considered to be worse. Bradykinesis was improved 50% or more in 22

(69%) patients. One (3%) patient's bradykinesis was worse and seven (22%) patients had equivalent bradykinesis when on combination therapy as contrasted to that with levodopa alone.

In two (6%) patients, dystonia was completely eliminated, but it was aggravated in ten (31%) patients and remained the same in seven (22%) patients.

Treatment with the combination of levodopa and carbidopa was discontinued in eight patients (20%) for reasons listed in Table II. Interestingly, the major complications of treatment, i.e., intractable gastrointestinal distress, psychiatric disorders, and abnormal involuntary movements, were infrequent causes for termination of therapy in this series. In fact no patient's therapy was stopped because of abnormal involuntary movements, yet complications of treatment were common (Table III). Dystonic movements, the side effect encountered most often, occurred in 17 (53%) patients. The second most frequent complication of treatment was nausea and anorexia, occurring in seven patients (22%). Psychiatric symptoms, including de-

TABLE I

RESULTS OF TREATMENT WITH CARBIDOPA AND LEVODOPA

(Related to observations when patients were on levodopa alone or were untreated)

	N	Improved				No change	Worse
		25%	50%	75%	100%		
Tremor	28	2	2	1	16	5	2
Rigidity	39	3	5	6	14	11	-
Bradykinesis	35	6	8	4	10	7	1
Dystonia	19	-	-	-	2	7	10

TABLE II

COMBINATION THERAPY DISCONTINUED

Reasons	N	%
Nausea and anorexia	2	5
Impaired equilibrium and falling	2	5
Esoph., oro-buccal and laryngeal spasms	2	5
Anxiety and depression	1	2.5
Drooling, intolerance	1	2.5
Forced crying	1	2.5
Freezing	1	2.5

pression, anxiety, and hallucinations, occurred in six patients (19%). The remainder of the complications of treatment were similar in incidence to those which occur when levodopa is used independently. Laboratory studies which reflect hematopoietic, renal and hepatic function demonstrated abnormalities similar to those which occur when levodopa is used alone.

Discussion

Although the cause of Parkinson's

TABLE III
COMPLICATIONS OF TREATMENT

Complication	N	%
Dystonia	17	53.1
Nausea and anorexia	7	21.9
Depression, anxiety	4 (1Marked)	12.5
Impaired equilibrium, falling	4	12.5
Hallucinations	2	6.3
Gout	2	6.3
Laryngeal, esophageal & oro-buccal spasms	2	6.3
Poor speech	2	6.3
Cold hands	1	3.1
Tremor	1	3.1
Bruxism	1	3.1
Drooling, general intolerance	1	3.1
Headaches	1	3.1
Occasional pre-syncope	1	3.1
Perspiring	1	3.1
Blurring vision, occasional strabismus	1	3.1
Dyspnea	1	3.1
Episodic bradykinesia	1	3.1
Forced crying	1	3.1
Freezing	1	3.1

disease remains ill defined, experimental evidence and clinical results, demonstrating improvement with levodopa therapy, suggest that a deficiency of dopamine may be an important factor. Thus, Vogt demonstrated that norepinephrine, a metabolite of dopamine, exists mainly in the hypothalamus and brain stem²². Subsequently, Montagu identified dopamine in brain²³. Bertler and Rosengren reported that dopamine has a preferential distribution in basal ganglia,²⁴ while Carlsson postulated that dopamine might have a role to play in the functioning of the basal ganglia²⁵. Barbeau searched for an abnormal metabolism of catecholamines, particularly dopamine, in Parkinson's disease²⁶ and demonstrated a decreased urinary excretion of dopamine in Parkinsonian patients²⁷. Previously Ehringer and Hornykiewicz had proven that brain dopamine was substantially reduced in Parkinson's disease²⁸. Anden, *et al* outlined a nigrostriatal dopaminergic pathway and suggested that dopamine may be

formed in the substantia nigra and transported thereafter to the striatum via that pathway²⁹.

The logical approach to the treatment of deficiency disorders is replacement of the substance in need. Since dopamine does not cross the blood brain barrier it is unavailable for entry into brain. Its precursor, levodopa, does enter brain where it is presumed to be decarboxylated to dopamine, the putative neurotransmitter.

Cotzias and co-workers added further credence to the theory that dopamine may be deficient in Parkinson's disease and confirmed the utility of treatment with its precursor by reporting satisfactory results with high doses of DL-dopa³⁰. Subsequently they proved that the active compound was the L-isomer of dopa². The fact that replacement therapy with levodopa is beneficial in the treatment of Parkinsonism has since been substantiated by independent reports^{1,3-7}.

Amongst the problems associated with the use of levodopa are the high daily doses required. Wurtman has shown that less than 0.1% of orally administered levodopa enters brain⁹. Hakanson and Owman reported that levodopa is metabolized in everted rat stomach⁸. Rivera Calimlim, *et al* confirmed those findings and indicated that a similar process occurs in human stomach¹¹. Bakke showed that *in vitro* dopa is metabolized by intestinal microflora to 3, 4, dihydroxyphenylacetic acid (DOPAC) which subsequently undergoes further changes³¹. In patients with hemigastrectomies, lower doses of levodopa have been required and higher plasma concentrations have been attained^{11,32}. Direct duodenal infusion of levodopa has been even more successful in attaining high plasma concentration¹¹. Finally, the kidney has been identified as a site of metabolism of levodopa³³.

These, and other observations, led to speculation that inhibition of extra-

cerebral L-aromatic amino acid decarboxylase would reduce peripheral metabolism of L-dopa enabling increased quantities to enter brain for further metabolism in surviving neurons of the nigrostriatal pathway. An agent which itself remains extracerebral and at ordinary doses has no intracerebral effect should be best. Carbidopa (L-alphamethyldopahydrazine) is such a drug³⁴.

In this series when carbidopa was used in combination with levodopa, a mean reduction of approximately 73% of previous orally administered levodopa doses occurred, and in many cases equivalent antiparkinsonian responses were attained. Similar results have been reported previously¹⁹⁻²¹. Notwithstanding, the incidence and severity of centrally mediated complications of treatment seemed to be the same or greater. This must obtain from the fact that the pharmacological actions of levodopa in brain remain the same, and that greater quantities are available centrally because of inhibition of its peripheral metabolism.

In other reports the frequency and severity of nausea and emesis have been reduced after the addition of carbidopa^{20,21,35,36}. By contrast, gastrointestinal distress, including nausea and anorexia, was the second most common complication in this series, and, in two patients, discontinuance of therapy was required because of those symptoms. The induction of nausea and vomiting is presumed to occur as a result of stimulation of the vomiting center, a medullary structure, by dopamine after its conversion from levodopa. Since it is outside the blood brain barrier, it is accessible to the entry and actions of carbidopa. Thus, by preventing or reducing decarboxylation of levodopa to dopamine in the vomiting center, intractible gastrointestinal distress may be reduced. To achieve that, however, larger doses of carbidopa, or smaller doses of levo-

TREATMENT OF PARKINSON'S DISEASE WITH CARBIDOPA

FERMAGLICH

dopa, than those administered to the group of patients in this report, are required. Thus, the mean levodopa:carbidopa ratio in Calne's series was less than 3:1,^{3,6} in Mars' patients approximately 8:1,²¹ and in the groups of Yahr²⁰ and Markham³⁵ about 10:1. In Georgetown University patients, the levodopa:carbidopa ratio was greater than 14:1. Yet in this group, centrally mediated complications of treatment were somewhat lower than in the four other studies, and more effective antiparkinsonian control was achieved. This leads to the conclusion that the higher doses of carbidopa, or the lower doses of levodopa required to suppress intractable gastrointestinal distress, result in the potentiation of centrally mediated complications or diminished antiparkinsonian control.

This study and review of recent literature demonstrates that the major utility of the addition of carbidopa to levodopa therapy in the treatment of Parkinson's disease is the reduction of total daily maintenance doses of levodopa. By varying the levodopa:carbidopa ratio, suppression of gastrointestinal distress, improvement of antiparkinsonian control and in selected cases, decrements in dystonic movements, may be achieved. Finally, in view of the reduction of total dose of levodopa, induction of therapy may be more rapid.

Acknowledgements

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References

1. BARBEAU, A.: L-dopa in Parkinson's disease: A critical review of nine years' experience. *Can. Med. Assoc.*, 101:791-800, 1969.
2. COTZIAS, G. C., PAPAVASILIOU, P. S., GELLEN, R.: Modification of Parkinsonism: Chronic treatment with L-dopa. *N. Engl. J. Med.*, 280:337-345, 1969.
3. YAHR, M.D., DUVOISIN, R. C., SCHEAR, M. J., *et al.*: Treatment of Parkinsonism with levodopa. *Arch. Neurol.*, 21:343-355, 1969.
4. MCDOWELL, F., LEE, J. E., SWIFT, T., *et al.*: Treatment of Parkinson's syndrome with L-dihydroxyphenylalanine (levodopa). *Ann. Int. Med.*, 72:29-35, 1970.
5. KLAWS, H.L., JR., GARVIN, J.S.: Treatment of Parkinsonism with L-DOPA (Study of 105 patients). *Dis. Nerv. Sys.*, 30:737-746, 1969.
6. CALNE, D. B.: L-DOPA in the treatment of Parkinsonism. *Clin. Pharm. Ther.*, 11:789-801, 1970.
7. COTZIAS, G. C.: Levodopa in the treatment of Parkinsonism. *JAMA*, 218:1903-1914, 1971.
8. HAKANSON, R., OWMAN, C.: Distribution and properties of amino acid decarboxylase in gastric mucosa. *Biochem. Pharmacol.*, 15:489, 1966.
9. WURTMAN, R. J., CHOU, C., ROSE, C.: The fate of C¹⁴ dihydroxyphenylalanine (C¹⁴DOPA) in the whole mouse. *J. Pharmacol. Exp. Therap.*, 174:351-356, 1970.
10. BIANCHINI, J. R., CALIMLIM, L. R., MORGAN, J. P., *et al.*: Metabolism and absorption of L-3, 4-dihydroxyphenylalanine in patients with Parkinson's disease. *Ann. N.Y. Acad. Sci.*, 179:126-140, 1971.
11. RIVERA-CALIMLIM, L. DUJOVNE, C. A., MORGAN, J. P., *et al.*: Absorption and metabolism of L-DOPA by the human stomach. *Europ. J. Clin. Invest.*, 1:313-320, 1971.
12. TYCE, G.: Metabolism of 3,4-dihydroxyphenylalanine by isolated perfused liver. *Biochem. Pharmacol.*, 20:3447-3462, 1971.
13. WURTMAN, R. J., ROMERO, J. A.: Effects of levodopa on nondopaminergic brain neurons. *Neurol.*, 22:72-81, 1972.
14. WURTMAN, R. J.: Effect of L-DOPA on S-adenosylmethionine levels and norepinephrine in rat brain. *Adv. Biochem. Psychopharm.*, 6:241-246, 1972.
15. SANDLER, M., CARTER, S. B.: Tetrahydroisoquinoline alkaloids: In vivo metabolites of L-DOPA in man. *Nature*, 241:439-443, 1973.
16. TISSOT, R., GAILLARD, J. M., GUGGISBERG, M. *et al.*: Therapeutique du syndrome de Parkinson parla L-DOPA "per os" associée a un inhibiteur de la decarboxylase (RO IV 46, 02). *Presse Medicale*, 77:619, 1969.
17. BARBEAU, A., GILLO-JOFFROY, L., MARS, H.: Treatment of Parkinson's disease with levodopa and RO 4-4602. *Clin. Pharmacol. Therap.*, 12 (part 2):353, 1971.
18. PAPAVASILIOU, P. S., COTZIAS, G. C., DUBY, S. E., *et al.*: Levodopa in Parkinsonism: Potentiation of central effects with a peripheral inhibitor. *N. Engl. J. Med.*, 286:8-14, 1972.
19. CHASE, T. N., WATANABE, A. M.: Methyl dopahydrazine as an adjunct to L-DOPA therapy in Parkinsonism. *Neurol.*, 384-392, 1972.
20. YAHR, M. D., DUVOISIN, R. C., MENDOZA, M. R., *et al.*: Modification of L-DOPA therapy of Parkinsonism by alphanemethyl dopahydrazine (MK-486). *Trans. Am. Neurol. Assoc.*, 96:55-58, 1972.
21. MARS, H. D.: Modification of levodopa effect by systemic decarboxylase inhibition. *Arch. Neurol.*, 28:91-95, 1973.
22. VOGT, M.: The concentration of sympathin in different parts of the central nervous system under normal conditions and after administration of drugs. *J. Physiol. (London)*, 123:451-481, 1954.
23. MONTAGU, K. A.: Catechol compounds in rat tissues and in brains of different animals. *Nature (London)*, 180:244, 1957.
24. BERTLER, A., ROSENGREN, E.: The occurrence and distribution of dopamine in brain and other tissues. *Experientia*, 15:10, 1969.
25. CARLSSON, A.: The occurrence, distribution and physiological role of catecholamines in the nervous system. *Pharmacol. Rev.*, 11:490, 1959.
26. BARBEAU, A.: Preliminary observations on abnormal catecholamine metabolism in basal ganglia disease. *Neurol.*, 10:446, 1960.
27. BARBEAU, A., MURPHY, G. F., SOURKES, T. L.: Excretion of

dopamine in diseases of basal ganglia. *Science*, 133:1706-1707, 1961.

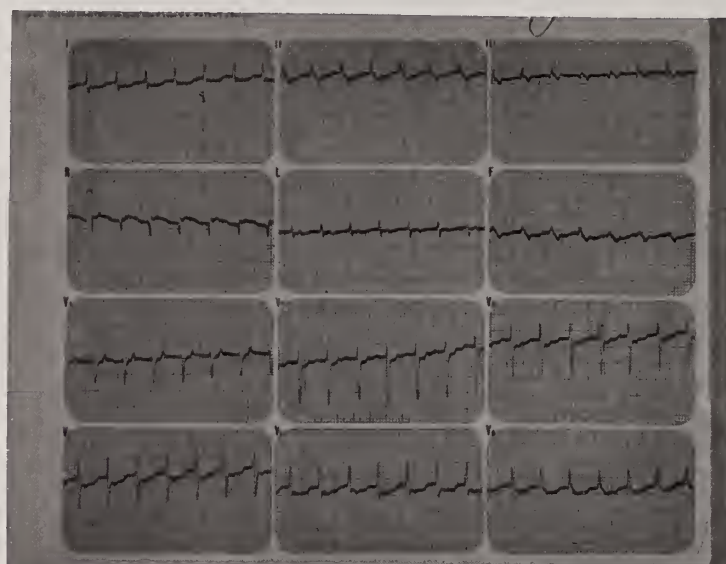
28. EHRINGER, H., HORNYKIEWICZ, O.: Verteilung von noradrenalin und dopamin (3-hydroxytyramin) im Gehirn des menschen und ihr Verhalten bei Erkrankungen des extrapyramidalen systems. *Klin. Wschr.*, 38:1236-1239, 1960.
29. ANDEN, N. E., CARLSSON, A., DAHLSTROM, A., *et al.*: Demonstration and mapping out of nigro-neostriatal dopamine neurons. *Life Sci.*, 1964, 3:523-530.
30. COTZIAS, G. C., VAN WOERT, M. H., SHIFFER, L. M.: Aromatic amino acids and modification of Parkinsonism. *New Engl. J. Med.*, 276:374-379, 1967.
31. BAKKE, O. M.: Degradation of Dopa by intestinal microorganisms in vitro. *Acta Pharmacol. Toxicol. (Kopenhagen)*, 30:115-121 (No. 1-2), 1971.
32. FERMAGLICH, J., O'DOHERTY, D. S.: Effect of gastric motility on levodopa. *Dis. Nerv. Sys.*, 33:624-625, 1972.
33. DAVIS, V. E., AWAPARA, J.: A method for the determination of some amino acid decarboxylases. *J. Biol. Chem.*, 235:124-127, 1960.
34. BARTHOLINI, G., PLETSCHER, A.: Effects of various decarboxylase inhibitors on the cerebral metabolism of dihydroxyphenylalanine. *J. Pharm. Pharmacol.*, 21:323-324, 1969.
35. MARKHAM, C. H., DIAMOND, S. G., TRECIOKAS, L. J.: Carbidopa in Parkinson's disease and in nausea and vomiting of levodopa. *Arch. Neurol.*, 31:128-133, 1974.
36. CALNE, D. B., REID, J., VAKIL, S., *et al.*: Idiopathic Parkinsonism treated with an extracerebral decarboxylase inhibitor in combination with levodopa. *Br. Med. J.*, 3:729-732, 1971.

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ECG PROBLEMS

HISTORY: A 56-year-old woman seen in the emergency room with a history of palpitation for one hour. Blood pressure 90/60.
(for diagnosis see page 602)



Transient Global Amnesia

HAROLD STEVENS, PH.D., M.D. AND BRUCE J. AMMERMAN, M.D.

Abstract

Transient global amnesia, an allegedly uncommon syndrome, is characterized by sudden spontaneous loss of memory, but with preservation of consciousness and self-identity. The eleven cases analyzed are representative of this easily recognizable entity. Typically, the attack was self-limiting; none had a recurrence. The neurological examination and EEG are usually normal. Dangerous and painful tests can be circumvented. Over-medication should be avoided.

The sudden spontaneous loss of memory in an otherwise active and healthy person is a dramatic event, frightening and puzzling to the physician as well as to the patient. This unique phenomenon, recently delineated, has been labeled "transient global amnesia."¹ Diagnosis is easy. Typically, profound amnesia appears suddenly in a middle-aged or older patient, without loss of consciousness. Keen awareness of their predicament is maintained and the victim persistently queries friends and relatives in a desperate effort to reconstruct the past events that elude him. The retrograde amnesia extends back from several hours to years, recedes spontaneously over a period of several hours, but leaves a memory gap of one or more hours which the patient is

Profound amnesia appears suddenly in a middle-aged or older patient, without loss of consciousness. . . . The retrograde amnesia extends back from several hours to years, recedes spontaneously over a period of several hours, but leaves a memory gap of one or more hours which the patient is never able to recall though during this interval his behavior and response may have been completely appropriate.

never able to recall though during this interval his behavior and responses may have been completely appropriate. The most unique and characteristic feature is the rarity of recurrences.^{2,3} The incidence of this syndrome is considered rare, with the usual implication that many cases go undiagnosed. Relatively few reported observations have been recorded on transient global amnesia, probably because of the too frequent erroneous inference that sudden amnesia in an otherwise healthy person is a hysterical fugue state.

The most recent report by Patten, published in 1971, states that of the thirty-six cases now known to the medical literature, only six have been examined by a physician during the

attack.⁴ We have studied eleven cases; two were examined during the attack. (Table I).

The following is illustrative of this entity, occurring in a sixty-three year old corporation lawyer nine years ago:

The episode began about 5 p.m. while the patient was conducting a meeting. He was able to finish chairing the meeting without the audience noticing anything out of the ordinary. Shortly thereafter he returned to his office and when addressed by his secretary failed to respond. At 6:15 p.m. he phoned his wife asking her to explain to him why he was at the office so late. He arranged for his wife to meet him in front of the building but the patient did not appear and his wife had to come upstairs to the office. She called a physician who found the patient confused, mildly agitated, perplexed, and patently frustrated by his failure to recall the events of that day. He kept asking "what is the matter?, this is ridiculous, assinine . . ." and repeatedly criticized himself for his helplessness and inability to reconstruct the events and to reorient himself. His wife drove him home. The following morning the patient was well, could recall dimly some of the events of the late evening before; however, he

TRANSIENT GLOBAL AMNESIA

STEVENS AND AMMERMAN

could not remember the meeting nor the events that preceded. After two days he could vaguely remember some of the events leading up to the meeting but nothing of the meeting at all. He was able to write in a few days a very exhaustive description of his feelings as well as a detailed account of his behavior as observed by the physician, his wife, and friends.

The neurological examination was negative aside from slight decrease in associated movements on the right side. Blood pressure was 150/100, the cerebrospinal fluid (CSF) was normal on the day after the incident. X-ray of the skull and brain scan were normal. The electroencephalogram (EEG) initially was diffusely abnormal, later showed a left anterior temporal focus,

and subsequently all EEG's have been normal. There have been no recurrences over the ensuing nine years and he remains active in his profession as a corporation lawyer.

Typically, the episode was spontaneous and transient, not associated with any physical or psychogenic precipitating factors. There was no aura, no seizure, and no loss of consciousness nor was there focal weakness, apraxia, aphasia or paresthesias; at no time did he demonstrate involuntary movements or incontinence. There was no loss of personal identity which is in contrast to hysterical fugue states. No confabulation nor perservation was manifest. Characteristically, during the attack the patient appeared perplexed and frustrated, desperately and persistently sought clarification and help in re-orienting

his memory and restoring temporal events to their appropriate place and sequence. Self identification remained intact as in the case of J. H., Age 55:

After the usual day of a nursery man, he came home and while sitting in a relaxed posture, suddenly was unable to recognize his surroundings. There were no known precipitating factors except he volunteers that he was agonizing over a complicated estimate on an extensive landscape project. He states "it was like everything was years away," realized that his son was a familiar person that he felt he knew years ago. He demanded to know why his twenty-nine year old son's hair was so long when actually it had been long for many years. He states "everything evaporated into

PATIENT	SEX	AGE	OCCUPATION	ESTIMATED DURATION OF:		EEG	ASSOCIATED FINDINGS	FOLLOW UP
				INITIAL AMNESIA	FIXED AMNESIA			
JD	M	60	ECONOMIST	1 WK	3 H	N	AMAUROSIS FUGAX 7 YRS LATER	15 YR
HG	M	48	WRITER	5 YR	7½ H	N		13 YR
OV	M	58	PHYSICIAN	8 H	1½ H	N		9 YR
AG	M	63	LAWYER	2 WK	3 H	ABN		9 YR
AD	F	64	SOC. WORKER	1 WK	2 H	ABN		3 YR
AB	M	43	GOVT. ADM.	1 WK	½ H	N		1 YR
GG	M	79	RETIRED	1 D	3 H	ABN		1 YR
AD	F	68	HOUSEWIFE	6 H	1 H	N	AMAUROSIS FUGAX 6 MO PREVIOUSLY x3	1 YR
EW	F	59	RETIRED	3 H	½ H	N		2 MO
TA	F	61	HOUSEWIFE	1 WK	4 H	N		5 MO
LS	F	55	CLERK-TYPIST	2 WK	2 H	N		16 MO

the distance, I knew what I had to do but knew that I couldn't think how to do it, I was conscious through the whole thing." He vainly struggled to reconstruct the events of the day, tried to think of his employees, "it was like I knew them years ago but there was not a vivid present thing." When asked regarding self identification and whether he knew who he was, his answer was vehement, "you're damn right I do." To his wife he stated "Helen, you seem to be a million years away." He then states he felt he was in a setting "like I just returned from a long interval, like I had to get reacquainted again." He became agitated over his frustration and when he saw his two month old Oldsmobile in the driveway, he demanded to know whose car it was. Another car, several years older, he readily recognized as his own. His symptoms receded in about four hours but that whole day remained hazy.

He had not been drinking, had not engaged in sexual intercourse for about a week and had been on no medication. The neurological examination was completely negative.

In most patients the neurological examination is negative and the laboratory tests are negative including the EEG. A few have shown abnormal EEGs^{1,3,5-10} as in the above patient and as in a sixty-four year old psychiatric social worker:

While eating lunch, she suffered a spontaneous amnesic episode, not associated with loss of consciousness, dysarthria or impairment of normal consecution of thought. However, during a telephone conversation, she demonstrated a memory deficit dating back one week. She has no recollection of

this call to this day and maintains an interval of amnesia that extends over about two hours. There was no incontinence, focal weakness, paresthesias nor ocular symptoms. The EEG showed a left frontotemporal focus of mild degree which resolved spontaneously and is now normal after two and a half years. There have been no recurrences.

We have surveyed the data on these eleven patients with transient global amnesia to determine if there was any consistent precipitating factor. None was found. As noted in the last case, the patient was eating lunch, but there is no consistent correlation with meals, emotion, or time of day except that most seem to appear from mid-morning to mid-afternoon. Possible precipitating circumstances have been recorded by others^{1,3} including severe emotion, exposure to cold, excessive heat, and prolonged abnormal posture of the head. Three cases reported in the literature^{3,9} and two in this series were preceded by sexual intercourse, as was the case with the following patient, a forty-three year old writer:

Several minutes after having sexual intercourse with his wife he went out into the yard to perform some non-arduous duties. He had no further recollection, said he was found in the kitchen by his wife and daughter who struggled to reorient him and restore his memory. He was later informed by his family that when he went out into the yard and saw a roll of fencing that he had purchased the day before he could not understand why the fencing was in his yard, demanded to know who put it there. He recognized and conversed coherently with his family but did not realize that his college age daughter had been home for a week, asked why she was not in school. The amnesia initially

extended back about one week, but after a period of several hours it constricted to about thirty minutes of which he still has no recollection. The EEG and the neurological examination were normal and there have been no recurrences during the eight month follow-up period.

An identical episode occurred in another man, also younger than the average age for this entity:

P. B., a forty-eight year old writer, while working in the garden at about 10:00 a.m. became agitated, came in the house, perplexed and sobbing. He asked his wife what was happening, complained that he lost a ring. Even after the ring was promptly located the patient remained implacable. He was examined immediately by a physician and some medication prescribed, but this made him increasingly restless and agitated so that heavy sedation was given. He would awake from time to time to repeatedly query his family, but by 5:30 in the evening his responses were normal and memory processes appeared intact. However, when the physician asked where he worked the patient gave a coherent appropriate answer except that he alluded to a job he had five years before. Prior to this episode the patient had arisen at his usual hour, had a hearty breakfast, and had read the newspaper. The amnesia promptly receded, remains static and fixed for a period of about two hours. Neurological examination and EEGs have been normal and there has been no recurrence.

The cardinal defect in transient global amnesia is the inability to lay down lasting memory traces with retention of significant remote memory and its read out mechanism^{7,8,11}. The patho-

TRANSIENT GLOBAL AMNESIA

STEVENS AND AMMERMAN

genesis of this unique entity has remained a matter of speculation. Some believe it is a form of seizure disorder⁹, possibly affecting the parahippocampal gyri, mamillary-hypothalamic region, brain stem, reticular system or the thalamus^{8,10}. Some suspect a temporary decrease in cerebral blood flow^{3,6,10,12}. Transient ischemia is implied by three cases which we have observed, two of whom have subsequently experienced amaurosis fugax which is another anatomically focal, transient, self limiting vascular phenomena. In addition, another patient suffered unilateral recurrent paresthesias several years after her transient global amnesic attack. All eleven patients are in good health, none had a recurrence.

The differential diagnosis would include mnemonic defects from trauma, seizures, alcoholism, hypoglycemia or other toxic-metabolic states^{10,13,14}. As stated, hysteria can be ruled out by the age of the patient and by maintenance of self-identity; typically, the hysterical patient either refuses to recognize or rejects his identity and, as stated, in hysteria immediate precipitating factors are usually apparent¹⁵. In functional amnesia the patient is usually young and there is usually an obvious psychological mechanism. Also, functional amnesia patients are usually relatively unconcerned over their illness, while by contrast patients with transient global amnesia are patently anxious, self critical, and struggle to reorient themselves and close the memory gap. Also, functional amnesias selectively involve loss of memory for personal and remote rather than recent events.

Experience with these eleven cases, as well as those reported in the literature, justifies an optimistic prognosis. In addition, one can safely circumvent the more dangerous and painful studies, such as pneumoencephalogram and arteriogram. The lat-

ter is particularly prone to produce accidents in patients vulnerable to cerebral vasospasm. Management should consist of reassurance and avoidance of over-medication. A negative neurological examination, and normal EEG and brain scan further validates the diagnosis.

Summary

Transient global amnesia is a readily recognizable entity, characterized by sudden spontaneous onset of amnesia, with preservation of consciousness and self-identity. The patient is keenly aware of his defect, struggles to regain his memory and reconstruct the mnemonic points of reference. Remote memory is preserved, neurological examination is negative and EEG usually normal. Prognosis is excellent, recurrences rare. Transient ischemia of the hippocampus or its connections is the probable cause. Reassurance only is required; over-medication should be avoided.

References

1. FISHER, C.M., ADAMS, R. D.: Transient Global Amnesia. *Acta Neurol. Scandinav.*, 1964, 40:7-83.
2. BENDER, M.B.: The Syndrome of Isolated Episode of Confusion with Amnesia. *Jour. of Hillside Hosp.*, 1956, 5:212-215.
3. BOLWIG, T.G.: Transient Global Amnesia. *Acta. Neurol. Scandinav.*, 1968, 44:101-106.
4. PATTEN, B.M.: Transient Global Amnesia Syndrome. *J.A.M.A.* 1971, 217:690-694.
5. JAFFE, R., BENDER, M. B.: EEG studies in the syndrome of isolated episodes of confusion with amnesia. *J. Neurol. Neurosurg. Psychiat.* 1966, 29:472-474.
6. POSER, C. M., ZIEGLER, D. K.: Temporary amnesia as a manifestation of cerebrovascular insufficiency. *Trans. Amer. Neurol. Assoc.* 1960, 85:221-223.
7. EVANS, J. H.: Transient loss of memory, an organic mental syndrome. *Brain* 1966, 89:539-548.
8. SHUTTLEWORTH, E. C., MORRIS, C. E.: The Transient global amnesia syndrome. *Arch. Neurol.* 1966, 15:515-520.
9. GODLEWSKI, S.: Amnesic episodes (transient global amnesia). *Sem Hop Paris* 1968, 44:553-577.
10. THARP, B.R.: The Electroencephalogram in transient global amnesia. *Electroenceph. Clin. Neurophysiol.* 1969, 26:96-99.
11. CREVEL, H. Van: Transient Global Amnesia. *Psych. Neuro. Neurochir.* 1969, 72:319-324.
12. STEVENS, H.: Strokes—transient and trivial. *Bull. Sibley Med. Assoc.* 1967, 10:3-9.
13. MAZZIA, V., RANDT, C.: Amnesia and eye movements in first stage of anesthesia. *Arch. Neurol.* 1966, 14:522-525.
14. KAHLER, R. L., BURROW, G. N., FELIG, P.: Diazepam—induced amnesia for cardioversion. *J.A.M.A.* 1967, 200:997-998.
15. STEVENS, H.: Conversion hysteria—a neurological emergency. *Proc. Mayo Clin. Bull.* 1968, 43:54-64.

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Selective Hypoaldosteronism: A Case Report and Review of Literature

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Abstract

This is a case report of selective hypoaldosteronism and a review of twenty-nine previously reported cases. Clinical manifestations are related to the effects of hyperkalemia on the cardiovascular and neuromuscular systems. The majority of patients are elderly and have either a previous history of hypertension, diabetes or mild to moderate renal insufficiency. These findings have important roles in the clinical presentation and possible pathogenesis of this condition in adults.

Introduction

The kidney, even when damaged, has a remarkable capacity for increasing potassium excretion. As a result, hyperkalemia is relatively uncommon in chronic renal failure. It is encountered most often in terminal renal failure, and in the presence of oliguria complicating extensive tissue destruction or hypercatabolic states. It may also develop following unrestrained dietary potassium intake, ill-advised parenteral administration of potassium, or with use of potassium retaining diuretics in patients with chronic renal disease.

Occasionally, hyperkalemia is ob-

Although some of the arrhythmias may be of supraventricular origin, the potential for the more serious ventricular dysrhythmias has been noted. The presence of arteriosclerotic heart disease may predispose patients to the toxic effects of hyperkalemia. The majority of these patients are elderly and significant arteriosclerosis of the coronary vessels is probably present.

served in chronic renal disease with no oliguria and only moderate azotemia. This has been described in patients with chronic pyelonephritis with hyperchloremic acidosis. The hyperkalemia was attributed to a defect in the renal tubular secretion of potassium.¹ Others have suggested that acidosis alters the normal ratio of intracellular to extracellular potassium with an increase in the extracellular component, so that in the presence of acidosis, extracellular concentration of potassium is high.² However, since most acidotic patients with chronic renal disease are not hyperkalemic, this mechanism is probably not a major factor.

In 1957, Hudson *et al*³ demonstrated low aldosterone secretion in a patient with hyperkalemia and cardiac conduction abnormalities. They at-

tributed the potassium retention to diminished aldosterone secretion. Since then, several cases of "selective hypoaldosteronism" have been published.⁴⁻²² The diagnosis is based on the demonstration of low aldosterone secretion without associated disturbances in other adrenocortical functions.

Case Report

This 35 year old black male was referred to the Medical Service of Freedmen's Hospital for evaluation of diabetes mellitus. He had intermittent blurring of vision since age 18, requiring correction for myopia. About a month prior to admission, he noticed rapid deterioration of vision in the left eye.

Diabetes mellitus had been discovered three years earlier at routine examination. A year earlier he was admitted to the hospital for removal of plantar warts of both feet. At that time, his fasting blood sugar ranged between 115 and 155 mg%, and an oral glucose tolerance test was consistent with diabetes mellitus. He weighed 14 lbs. 9 oz. at birth and had no siblings. There was a strong family history of diabetes; his father, all maternal aunts, a grand aunt and a cousin had the disease. His father died

SELECTIVE HYPOALDOSTERONISM

CRUZ, DILLARD AND HOSTEN

of kidney disease, and his mother died shortly after giving birth to this patient.

Physical examination revealed a well-developed, obese man. His blood pressure was 160/90, the pulse 80 per minute, respirations 14 per minute, and weight 210 pounds. The optic fundi showed bilateral neovascularization, with microaneurysms and large hemorrhages in the right eye plus a small visual defect. The left eye had a central visual field defect. The lungs, heart and abdomen were normal. There was ankle edema plus decreased tactile and vibratory sensations in both legs, without muscle atrophy. Deep tendon reflexes were normal. Plantar warts were present on both feet. Laboratory results: Hematocrit 33, hemoglobin 11.4, white blood cell count 6700 with 46% neutrophils, 43% lymphocytes, 2% monocytes and 9% eosinophils. The blood sugar was 112-183 mg%, blood urea nitrogen 43 mg%, serum creatinine 3.2 mg%, serum uric acid 7.7 mg%, sodium 136 meq/l potassium 5.8-6.7 meq/l, chloride 104 meq/l, bicarbonate 24 meq/l, cholesterol 200 mg%, total protein 6.5 gm%, albumin 3.3 gm% and globulin 3.2 gm%. On urinalysis, the pH was 5, specific gravity 1.010, protein 1+. There was no sugar or acetone, there were 3-4 WBC and rare RBC/hpf, a few granular casts. Twenty four hour urine protein was 780 mg. Endogenous creatinine clearance was 34 cc/min.

Method of Study

The patient was initially placed on a diet containing 17 meq of sodium [Na] (low Na diet) daily. A twenty four hour urine specimen was collected on the 5th day for an aldosterone level, and plasma was obtained for renin activity after four hours of upright posture. His diet was then changed to allow unrestricted sodium intake. In addition he received 102

meq of supplemental sodium daily (high Na diet). Plasma renin activity and urinary aldosterone levels were measured on the 5th day of high salt intake.

Twenty four hour urine samples were also collected for sodium, potassium, 17-hydroxycorticosteroids and 17-ketosteroids. A 24 hour collection for 17-hydroxycorticosteroids was repeated after ACTH stimulation. Sodium and potassium were measured by internal standard flame photometer. Urinary and plasma 17-hydroxycorticosteroid and 17-ketosteroid were measured as Porter-Silber chromogens. Plasma renin activity and urinary aldosterone concentration were measured by the method of Haber^{2,3} and of Mayes^{2,4} respectively.

Results

- A. I. Electrolyte excretion: While on the high Na diet, the patient's urinary sodium was 124 meq and urinary potassium was 46 meq per 24 hours. When his Na intake was restricted to 17 meq/day, his urinary Na excretion was 116 meq and the urinary K excretion was 42 meq per 24 hours.
- II. Adrenal steroids excretion: On the high Na diet, the twenty four hour urinary excretion of 17-hydroxycorticosteroid was 17.8 mg (normal 9-25 mg), and of 17-ketosteroid was 15.3 mg (normal 9-22 mg). Following infusion of 40 units of ACTH over 8 hours, the urinary excretion of 17-hydroxycorticosteroid rose to 54.4 mg.
- III. Aldosterone excretion: Urinary aldosterone excretion was 3.4 μ g/24 hrs. on the high sodium diet (normal 5-19 μ g/24 hrs.) and 8.2 μ g/24 hrs. on the low sodium diet (normal 20-60 μ g/24 hrs.).

- IV. Plasma renin activity: After 5 days of low Na intake and 4 hours of upright posture, the plasma renin activity was 11 μ g/hr. (normal 30-230 μ g/hr.). After 5 days of high Na intake, the plasma renin activity was 9 μ g/hr. (normal 30-120 μ g/hr.). The serum potassium was 6.7 meq/l when the specimen for renin was collected during sodium restriction and was 6.3 meq/l when the specimen was collected during sodium supplementation. The patient was then returned to sodium restriction for 1 week and sodium polyesterene resin was given. A plasma renin activity repeated when the serum potassium was 4.8 meq/l, was 11.6 μ g/hr.

Review of Literature

There are twenty nine cases of selective hypoaldosteronism in adults reported in the literature plus the case reported here. Most of the cases occurred in the elderly, with 16 patients over age 60. Mean age of the 30 cases was 61 (range 18-82).

Presenting complaints were related to the central nervous system and the cardiovascular system. Weakness, dizziness and syncope were the predominant complaints. Convulsive seizures occurred in three patients. Muscular cramps, stiffness and muscle twitching were seen in a few patients. One presented with periodic paralysis of the extremities. Eight patients were asymptomatic.

Postural hypotension was observed in thirteen patients. Six were admitted with evidence of congestive heart failure. Hypertension was present either on admission or by history in nine patients. Five patients had myocardial infarction. Angina pectoris, peripheral arterial insufficiency, and

pulmonary embolism were each encountered once.

Electrocardiograms were normal in nine patients and abnormal in nineteen. Ten of these showed serious arrhythmias. Five had complete heart block and another four had other types of conduction abnormalities. Supraventricular tachyarrhythmias were seen in four patients and two patients had severe sinus bradycardia. Only five patients showed peaked T waves.

Evidence of renal disease in the form of azotemia or proteinuria was present in 26 cases. Glomerular filtration rate measured by inulin, creatinine or urea clearance was given in twenty four patients, and was normal in eight, and reduced in sixteen patients. Mean creatinine clearance was 71 cc/min. with a range of 22 to 151 cc/min. Azotemia was present in twenty one patients, and was minimal in seventeen and moderately severe in four. Mean BUN was 32 mg% with a range of 12 to 104 mg%. Proteinuria was present in ten patients and was over 3 gm/24 hrs. in three patients, one of whom was grossly nephrotic secondary to renal vein thrombosis.

Causes of the renal disease were variable. Obstructive lesions involving the urethra, prostate, or ureter were found in four patients. Six patients had a renal biopsy. Nephrosclerosis was the predominant finding in four of these. The kidney was histologically normal in the other two, except that one of these had a marked increase in the juxtaglomerular cell index.

Serum potassium was elevated in 25 patients and was normal in five patients. The mean value was 6.6 meq/l with a range of 3.5 to 9.0 meq/l. In twenty patients urinary sodium exceeded intake. However, only 13 had serum sodium concentrations below 135 meq/l. Hyperchloremic metabolic acidosis was observed in nine patients.

A significant finding in this review is the presence of diabetes mellitus in

nine cases, and the presence of elevated fasting blood glucose or abnormal glucose tolerance test in another three patients. Two patients had associated gout and another two patients had hyperparathyroidism.

Discussion

The clinical features of selective hypoaldosteronism are related to abnormalities of the neuromuscular and cardiovascular system. Manifestations of cerebral hypoxia such as dizziness, weakness, and syncope are frequently seen and are the result of low cardiac output from hypovolemia or cardiac arrhythmias. Although some of the arrhythmias may be of supraventricular origin, the potential for the more serious ventricular dysrhythmias has been noted. The presence of arteriosclerotic heart disease may predispose patients to the toxic effects of hyperkalemia. The majority of these patients are elderly and significant arteriosclerosis of the coronary vessels is probably present. In addition, many of these patients had hypertension or diabetes mellitus, diseases which also predispose to the development of coronary artery disease. Indeed, five patients had myocardial infarction.^{3,9,10,12,19}

Mild to moderate renal insufficiency is another common finding in selective hypoaldosteronism. Azotemia in some was transient and probably reflected volume depletion. In others, the renal insufficiency was probably due to the effects of aging, hypertension, diabetes or lower tract obstruction.

It is accepted that hyperkalemia is unusual in mild renal insufficiency. Even in the presence of progressive chronic renal disease, the potassium balance is well maintained despite variations in dietary intake of potassium.²⁵ Experimentally, in dogs whose glomerular filtration rate is

reduced by partial infarction of one kidney, the surviving nephrons increase their potassium excretion significantly. This suggests the existence of a control mechanism capable of appropriately regulating the rate of potassium excretion per nephron to maintain potassium balance.²⁶ The exact mechanism for this adaptation is incompletely understood but aldosterone may play a role.²⁷ Thus, a trend to potassium retention is not surprising in selective aldosterone deficiency.

The mechanism for the aldosterone deficiency has not been fully explained. Generalized adrenal insufficiency is unlikely because, in all cases where tested, 24 hour excretion of 17-hydroxy and 17-ketosteroids was normal, as was the response to ACTH stimulation. Visser and Cost showed that in infants, the low aldosterone production was due to an enzymatic defect in aldosterone synthesis.²⁸ Posner *et al* suspected a defect in the 18-aldolase system of an 18 year old male who presented with periodic paralysis.⁸ They noted an increase in the urinary tetrahydrocorticosterone which rose further after administration of corticotrophin, while aldosterone was not detected in the urine. Wilson suggested that prolonged therapy with heparin could interfere with aldosterone synthesis and secretion.⁹ He demonstrated this in his patient whose adrenal zona glomerulosa was markedly thinned, and whose juxtaglomerular cell index was markedly increased. Disturbance in the autonomic nervous system was implicated as a cause of isolated reduced aldosterone secretion by Thomas and Shields¹⁵.

Another mechanism that could explain the isolated aldosterone deficiency is a defect in renin secretion, since renin is a strong regulatory factor in aldosterone production. As shown by previous reports,^{17,19,20} and in our patient, the plasma renin activity remained subnormal even with

SELECTIVE HYPOALDOSTERONISM

CRUZ, DILLARD AND HOSTEN

maneuvers such as sodium depletion and upright posture. An elevated plasma renin activity would be expected if the primary defect in hypoaldosteronism is within the adrenal cortex. This hypothesis is supported by the finding of elevated renin in Addison's disease and in infants with enzymatic defects in aldosterone production.^{2,8} Of the patients reviewed in this report, 77% with plasma renin measurements had low levels, suggesting that the low levels of aldosterone were secondary to defects in renin secretion.

Why plasma renin activity is low in most of these patients is still not known. Most of the reasons given are purely speculative. Renin substrate was normal in cases where it was measured.^{1,7} In some essential hypertensives, there is physiologic inhibition of renin release^{2,9} but only a third of the patients reported with selective hypoaldosteronism were hypertensive. Chronic lead intoxication was also found to inhibit renin and aldosterone excretion.^{3,0} However, in none of the patients in this review was a history of lead ingestion elicited. Hyperkalemia is also known to cause suppression of plasma renin activity^{2,5}. This is unlikely to be the sole cause since plasma renin activity remained low even in the presence of normal serum potassium in our patient and in some reported by others^{1,6,17,19,20}. Besides, sodium depletion is a greater stimulus to renin secretion and should overcome the suppressive effect of hyperkalemia^{2,5}. Finally, it has been suggested that renal disease has injured the juxtaglomerular apparatus producing a primary disturbance in the synthesis of renin¹⁷.

Arteriosclerosis may be an important factor in the pathogenesis of this condition. It may be responsible for the renal disease seen in these patients, and, by damaging the afferent arterioles and the juxtaglomerular ap-

paratus, be responsible for the low renin production. If the coronary arteries are involved, the accompanying coronary insufficiency would contribute to the deleterious effect of hyperkalemia on the conduction system. This would explain why most cases are reported in individuals who are either hypertensive, diabetic or elderly, three conditions associated with significant arteriosclerosis of both cardiac and renal vasculature.

There is another plausible reason why hyperkalemia is prone to occur in this group. An extrarenal mechanism for maintenance of potassium balance in chronic renal failure was described by Gonick^{3,1}. He found that patients with glomerular filtration rates of less than 30 cc/min. when given exogenous potassium, had an increase in plasma potassium concentration of only 1.21 meq/l, despite excreting only 9% of the administered potassium. This increase was not significantly different from the value of 1.05 meq/l observed in normals, who when given identical amounts of potassium, excreted 46% of the load. Hiatt *et al*^{3,2} performing similar experiments in animals, suggested the presence of an insulin-dependent extrarenal mechanism for transferring potassium from extracellular to intracellular fluid. Santeusano *et al*^{3,3} suggest that there may be a feedback control relationship between insulin and potassium. Using dogs, they demonstrated that increasing serum potassium concentration independently increased both insulin and glucagon secretion rates. The increased insulin concentration caused a fall in serum potassium due to potassium shifts into the intracellular fluid. Glucagon has no effect on potassium balance, but was thought to provide enough endogenous glucose to prevent hypoglycemia from increased insulin levels. If potassium homeostasis is dependent on both insulin and aldosterone secretion, it is not surpris-

ing to see hyperkalemia more often in diabetic patients with even mild renal failure. It seems a reasonable speculation that diabetes (1) contributes to the renal structural changes leading to low renin and aldosterone secretion, (2) promotes structural changes in the cardiovascular system that are conducive to potassium toxicity, and (3) interferes with extrarenal protection from hyperkalemia. Selective hypoaldosteronism therefore may not be rare, and should be suspected in elderly diabetics with renal involvement. Thus, the complications of severe hyperkalemia in this group may be prevented.

References

1. CARROLL, H. J., FARBER, S. J.: Hyperkalemia and hyperchloremic acidosis in chronic pyelonephritis. *Metabolism* 1964, 13:808-817.
2. BURNELL, J. M., VILLAMIL, M. F., UYENO, B. T., SCRIBNER, B. H.: The effect in humans of extracellular pH change on the relationship between serum potassium concentration and intracellular potassium. *J. Clin. Invest.* 1965, 35:935-939.
3. HUDSON, J. B., CHOBANIAN, A. V., RELMAN, A. S.: Hypoaldosteronism: a clinical study of a patient with an isolated adrenal mineralocorticoid deficiency, resulting in hyperkalemia and Stokes-Adams attacks. *N. Eng. J. Med.* 1957, 257:529-536.
4. SKANSE, B., HOKFELT, B.: Hypoaldosteronism with otherwise intact adrenocortical function, resulting in a characteristic clinical entity. *Acta Endocrinol (Kbh)* 1958, 28:29-36.
5. HILL, S. R., Jr., NICKERSON, J. F., CHENAULT, S. B., *et al*: Studies in man on hyper- and hypoaldosteronism. *Arch. Intern. Med.* 1959, 104:982-994.
6. LAMBREW, C. T., CARVER, S. T., PETERSON, R. E., *et al*: Hypoaldosteronism as a cause of hyperkalemia and syncopal attacks in a patient with complete heart block. *Am. J. Med.* 1961, 31:81-85.
7. RICK, W., WINKLER, G., KOCH, E., *et al*: clinical observations in hypoaldosteronism. *Acta Endocrinol. (suppl) (Kbh)* 1962, 67:103.

8. POSNER, J. B., JACOBS, D. R.: Isolated aldosteronism. I. Clinical entity, with manifestations of persistent hyperkalemia, periodic paralysis, salt losing tendency and acidosis. *Metabolism* 1964, 13:513-521.
9. WILSON, I. D., GOETZ, F. C.: Selective hypoaldosteronism after prolonged heparin administration. A case report, with postmortem findings. *Am. J. Med.* 1964, 36:635-640.
10. GERSTEIN, A. R., KLEEMAN, C. R., GOLD E. M. *et al*: Aldosterone deficiency in chronic renal failure. *Nephron*. 1968, 5:90-105.
11. VAGNUCCI, A. H. Selective aldosterone deficiency. *J. Clin. Endocrinol. Metab.* 1969, 29:279-289.
12. McGIFF, J. C., MUZZARELLI, R. E., DUFFY, P. A., *et al*: Interrelationship of renin and aldosterone in a patient with hypoaldosteronism. *Amer. J. Med.* 1970, 48:247-253.
13. VAGNUCCI, A. H.: Selective aldosterone deficiency in chronic pyelonephritis. *Nephron*. 1970, 7:524-537.
14. FERRARA, E., WERK, E., HANENSON, I., PRIVITERA, P., KENYON, C.: Selective hypoaldosteronism with blunted renin activity responsiveness. *Clin. Res.* 1970, 18:602.
15. THOMAS, J. P., SHIELDS, R.: Associated autonomic dysfunction and carcinoma of the pancreas. *Br. Med. J.* 1970, 4:32.
16. PEREZ, G., SIEGEL, L., SCHREINER, G. E.: Selective hypoaldosteronism with hyperkalemia. *Ann. Intern. Med.* 1972, 76:757-763.
17. SCHAMBELAN, M., STOCKIGT, J. R., BIGLIERI, E. G.: Isolated hypoaldosteronism in adults. *N. Engl. J. Med.* 1972, 287:573-578.
18. MELLINGER, R. C., PETERMANN, F. L., JURGENSON, J. C.: Hyponatremia with low urinary aldosterone occurring in an old woman. *J. Clin. Endocrinol. Metab.* 1972, 34:85-91.
19. WEIDMANN, P., REINHART, R., MASSRY, S. G. *et al*: Syndrome of hyporeninemic hypoaldosteronism and hyperkalemia in renal disease. *J. Clin. Endocrinol. Metab.* 1973, 36:965-977.
20. BROWN, J. J., CHINN, R. H., FRASER, R., LEVER, A. F., MORTON, J. J., ROBERTSON, J. I. S., TREE, M., WAITE, M. A., PARK, D. M.: Recurrent hyperkalemia due to selective aldosterone deficiency: Correlation by angiotensin infusion. *Br. Med. J.* 1973, 1:650-654.
21. GOLDFARB, S., SINGER, I., RELMAN, A. S., STRUNK, B., GOLDBERG, M.: Hyperglycemia induced hyperkalemia, diabetes and hypoaldosteronism. *Amer. Soc. Nephrol. (abs)* 1973, 42.
22. GOSAIN, V. V., FERRARA, E. V., Werk, E. E., *et al*: Impaired renin responsiveness with secondary hypoaldosteronism. *Arch. Intern. Med.* 1973, 132:885-890.
23. HABER, E., KOERNER, T., PAGE, L., KLIMAN, B., PURNODE, A.: Application of a radio immunoassay for angiotensin I to the physiologic measurements of plasma renin activity in normal human subjects. *J. Clin. Endocr.* 1969, 29:1349-1355.
24. MAYES, D., FURUYAMA, S., KEM, C., NUGENT, A.: A radioimmunoassay for plasma aldosterone. *J. Clin. Endocr.* 1970, 30:682-685.
25. BRUNNER, H. R., BAER, L., SEALEY, J. E. *et al*: The influence of potassium administration and of potassium deprivation on plasma renin in normal and hypertensive subjects. *J. Clin. Invest.* 1970, 49:2128-2138.
26. SCHULTZE, R. G., TAGGART, D. D., SHAPIRO, H. *et al*: On the adaptation in potassium excretion associated with nephron reduction in the dog. *J. Clin. Invest.* 1971, 50:1061-1068.
27. MILLS, J. N., TOMAS, S., WILLANSON, K. S.: The effects of intravenous aldosterone and hydrocortisone on the urinary electrolytes of the recumbent subject. *J. Physiol.* 1961, 156:415-423.
28. VISSER, H. K., COST, W. S.: A new hereditary defect in the biosynthesis of aldosterone: Urinary C21 corticosteroid pattern in three related patients with salt losing syndrome, suggesting an 18 oxidation defect. *Acta. Endocr.* 1964, 47:589-612.
29. JOSE, A., CROUT, J. R., KAPLAN, N. M.: Suppressed plasma renin activity in essential hypertension. *Ann. Intern. Med.* 1970, 72:9-16.
30. SANDSTEAD, H. H., MICHELAKIS, A. M., TEMPLE, T. E.: Lead intoxication. Its effect on the renin aldosterone response to sodium deprivation. *Arch. Environ. Health* 1970, 20:356-362.
31. GONICK, H. C., KLEEMAN, C. R., RUBINI, M. E., MAXWELL, M. A.: Functional impairment in chronic renal disease: III Studies of potassium excretion. *Am. J. Med. Sci.* 1971, 261:281-290.
32. HIATT, N., MARGENSTERN, L., DAVIDSON, M., BONARRIS, G., MILLER.: Role of insulin in the transfer of infused potassium to tissue. *Horn. Meta. Res.* 1973, 5:84.
33. SANTEUSANIO, F., FALOONA, G., KNOCH, J., UNGER, R.: Evidence for a role of endogenous insulin and glucagon in the regulation of K homeostasis. *J. Lab. Cl. Med.* 1973, 81:809-817.

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ECG PROBLEMS

(from page 592)

INTERPRETATION: 1. Paroxysmal supraventricular tachycardia.

This tracing shows completely regular QRS complexes at a rate of 166 per minute. The QRS interval is .06 second, identifying a supraventricular origin of the rhythm with normal intraventricular conduction. Each QRS complex is followed by a sharp deflection in the ST segment which represents a retrograde P wave. These are clearly seen in V_1 and lead II. Their timing, following the QRS complexes, and their retrograde contour (inverted in the leads II and aVF and upright in aVR) suggests that the rhythm arises in the A-V junction. The junctional focus appears to fire the ventricles first. Since the impulse reaches the ventricles from the A-V junction, the conduction within the ventricles can be normal. The impulse appears to reach the atria a little later, accounting for the fact that the P waves are written after the QRS complexes. The impulse spreads through the atria from the A-V junction in a direction exactly the reverse of the usual atrial depolarization, producing the inverted P waves. This is a supraventricular tachycardia, apparently arising in the A-V junction rather than in the atria.

Edited by Robert R. Montgomery, M.D.

SPECIAL ARTICLE

Public Behavior During an Air Pollution Episode: Implications for Health Planning

MELBA PRICE, B.A. AND BAILUS WALKER, JR., M.S.P.H.

Abstract

A simple survey was conducted in the District of Columbia to ascertain public behavior during an air pollution episode, which occurred in the Washington metropolitan area in July, 1973. The results of this survey indicate a reluctance on the part of metropolitan residents to change their behavior pattern (i.e., mode of transportation) during the air pollution alert. It is also apparent that existing methods of obtaining public support during an alert are insufficient to induce changes in habits, attitudes and behavior with regard to those factors which contribute to levels of pollution.

Introduction

Public support is a fundamental prerequisite for planning and implementation of environmental management programs. The public is involved to a greater or lesser degree in the definition of national goals, the specification of standards, the formulation of public plans and policies, efforts to alter values, attitudes and behavior and the assessment of their results. Unless a public demand exists for changes in attitude and in willingness to accept new goals there can be

It is evident that the mere announcement on radio and in the newspaper of an air pollution episode (alert stage) is not sufficient to motivate changes in habits, attitudes and behavior with regard to those factors which contribute to levels of pollution.

little perceptible improvement in the quality of our environment.

Recognizing this need, the District of Columbia Environmental Health Administration undertook a simple survey to determine the reaction of residents in the metropolitan area to a well-publicized period of intense air pollution—July 8 thru 10, 1973. Specifically, this study attempted to analyze the behavior of residents of the Washington metropolitan area to determine:

- a. Attitude toward air pollution alerts;
- b. Adherence to requests by Metropolitan Washington Council of Governments (COG) to curtail the use of their automobiles;
- c. Whether existing warning methods by COG are sufficient to awaken the residents to the seriousness of air pollution.

While certainly not definitive or exhaustive, the study provides useful indicators for carrying forward the District's mandate under the Clean Air Act of 1970.

Effects of Air Pollution Episodes

An air pollution episode is defined as an atmospheric condition in which ambient concentrations of airborne contaminants tend toward levels that imminently and substantially endanger the health of persons who are exposed to the air.

While there are no available clinical data on the specific effects of air pollution episodes on residents of metropolitan Washington, D.C., studies of other communities suggest that certain groups are more susceptible than others to the effects of these episodes.

The episode of air pollution that occurred in Belgium in 1930^{1,2} was the first one to be closely studied. The major symptoms observed were cough, dyspnea, wheezing, chest and rib pain, nausea and vomiting and, in the most severely affected, shock and death. Autopsies revealed extensive irritation and inflammation of mucous membranes, especially in the lungs, and frequent evidence of heart failure.

During the 5-day episode in

PUBLIC BEHAVIOR DURING AIR POLLUTION

PRICE AND WALKER

Donora³, 20 persons died, although only one or two deaths would have been expected during that interval. More than 40% of the general population (more than 5,900 persons) had symptoms, often on the very first day of the smog. If the same mortality and morbidity rates were applied to a city the size of New York, more than 10,000 deaths and more than three million illnesses would have occurred. Symptoms and autopsy results in Donora were similar to those in Belgium.

The London episode of 1952⁴—caused 4,000 more deaths than would normally have been expected. The mortality rate began to rise on the first day of the smog.

Studies of several subsequent episodes in London and in New York City clearly demonstrate that air pollution episodes lasting several days are accompanied by increases in mortality, in symptoms, or in frequency of clinical visits among certain groups of susceptible patients, especially those with cardiovascular or respiratory diseases.

In short, information from clinical, autopsy, and mortality studies demonstrate that:

- There is excess mortality and cardiorespiratory morbidity during air pollution episodes;
- The health effects of air pollution begin as soon as the smog occurs;
- Certain groups are far more susceptible than others to the effects of these episodes.

Episode Stages

There are three episode stages: ALERT, WARNING, and EMERGENCY.

An alert stage is declared when any one of the major pollutant concentrations is measured at any monitoring site, and due to adverse meteorological conditions can be expected to remain

at these levels or higher for the next twelve hours or more. Table 1 shows the pollutant levels at which air pollution episodes are declared.

The number of alerts declared in the Washington metropolitan area from 1970 to 1973 are as follows:

1970—3 alerts

1971—7 alerts

1972—5 alerts

1973—7 alerts

When air pollution standards of particular pollutants have been exceeded in D.C., the D.C. Environmen-

TABLE I

STAGES OF AIR POLLUTION EPISODES & POLLUTANT LEVELS

POLLUTANT	ALERT	WARNING	EMERGENCY
Sulfur Dioxide SO ₂	0.3 ppm* (24 hours)†	0.6 ppm (24 hours)	0.8 ppm (24 hours)
Carbon Monoxide CO	15 ppm (8 hours)	30 ppm (8 hours)	40 ppm (8 hours)
Oxidant Ox	0.1 ppm (1 hour)	0.4 ppm (1 hour)	0.6 ppm (1 hour)
Nitrogen Dioxide NO ₂	0.6 ppm (1 hour) 0.15 ppm (24 hours)	1.2 ppm (1 hour) 0.3 ppm (24 hours)	1.6 ppm (1 hour) 0.4 ppm (24 hours)

* parts per million

† average

tal Health Administration informs the Metropolitan Washington Council of Governments, a regional body consisting of representatives from all the jurisdictions in the Washington metropolitan area, who officially declares an air pollution alert for the metropolitan area.

When an alert is declared, the following actions are expected of the metropolitan region:

1. Restriction of solid waste incineration.
2. No open burning.

3. Curtailment of unnecessary use of automobiles, especially during peak traffic hours.
4. Use of public transit.
5. Reduction in sightseeing tours and the preparation of recreational facilities for an early closing.
6. Restriction of gasoline and diesel oil deliveries to service stations and industrial centers, with 50% reduction in the transfer of diesel and fuel oil, gasoline and kerosene from tanks to tank trucks.

Method

The findings reported in this paper come from interviews of 800 residents of the metropolitan area who were in an area of downtown Washington, bounded on the south by Pennsylvania Avenue, N.W., on the north by F Street, N.W., on the east by North Capitol Street and on the west by 19th Street, N.W. Persons interviewed were going to or from work, shopping or conducting personal business in the area. Twelve parking facilities, four department stores, five office buildings, stores, and Federal and District government office buildings were convenient locations for obtaining the desired information.

Environmental corpsmen and volunteer workers of the D.C. Environmental Health Administration conducted the interviews. The interviewing procedure and recording of responses were standardized. Pre-testing uncovered several ambiguities in wording and in design. These were corrected and the final questionnaire was developed.

The next task was to delineate the exact area in which the interviewing was to be conducted. The selection of downtown Washington, although essentially arbitrary, was based on convenience, and the likelihood of interviewing a reasonable cross-section of

the metropolitan area, especially the commuting work force as well as leisure shoppers.

The site selection was followed by a consideration of the random selection of persons in the designated area. In order to do this a commonly accepted method of random probability sampling was utilized (patterned after the survey technique by Backstrom and Kirsch in "Survey Design").

Minimum and maximum limits for our sample size were set and then adjusted to the most feasible number between the two. It was felt that a sample containing a minimum of 750 interviews was essential. The outside feasible maximum considering factors of time and manpower was put at 1,000.

Data Processing and Analysis

Although attempts were made to pre-code the questionnaires, it was determined that the most economical approach was hand tabulation. One person (MP) did all the tabulation and analysis to insure continuity and homogeneity.

Results

We wish to issue a few words of caution in reporting these simple tabulations, to prevent exaggeration and misinterpretation; both are vices which are all too prevalent and which, in fact were factors that prompted this study. First, this study can in no way be considered a study of the whole metropolitan area. It is a "random sample" of persons in the downtown area of the District of Columbia. The persons interviewed may be representative of the Washington metropolitan area as a whole or they may not. Second, it should be kept in mind that this survey took place at a certain point in time. Third, a simple tabula-

tion does not present a complete picture of survey results. It consists only of a summation of the numbers and percentages of persons who responded to various categories of particular questions.

Finally, several of the questions in this survey were open ended and required the respondents to explain why they felt as they did. These explanations which could not be coded often provided insight into problems covered by the questions.

As seen in Table 2, 30% of those interviewed had knowledge of the alert on the first day it was announced. Since it occurred on Sunday many of the area residents were at nearby resorts or beaches and did not learn of the air pollution problem until they returned home late Sunday night or Monday morning. Twenty-two percent of those having knowledge of the alert on Sunday indicated listening to hourly news reports on local radio stations.

Thirty-five percent of those who first learned of the alert on Monday said that they "occasionally" listen to radio newscasts but read, daily, at least one of the two major Washington newspapers, and identified these as the sources of their "air pollution" information.

Responses to questions on modes of transportation were interesting. Fifty-five percent of the respondents who live in the District of Columbia normally travel to work or go shopping by bus. During the air pollution episode there was no change in this pattern. Car pooling is not as popular in D.C. as it is in the Maryland and Virginia suburbs, but during the alert 26% of D.C. residents participated in car pools of two or more persons. (1.4 persons per car is the average ridership in the District during "normal" periods). However, ten percent of those who joined car pools did so for reasons other than the air pollution episode.

PUBLIC BEHAVIOR DURING AIR POLLUTION

PRICE AND WALKER

TABLE 2

Knowledge of Air Pollution Episode

QUESTION: When were you aware that the Washington metropolitan area was experiencing an air pollution alert?		
RESPONSE:		
	Number	Percent
The first day of the alert (Sunday)	240	30
The second day of the alert (Monday)	400	50
After the alert	152	19
Not informed	8	1
TOTAL	800	100

TABLE 3

Normal Mode of Transportation

QUESTION: How do you normally travel to work and to shop?						
RESPONSE:						
	Place of Residence					
	D. C.		Maryland		Virginia	
Mode of Transportation	No.	%	No.	%	No.	%
Bus	165	55	48	16	40	20
Car Pool	45	15	162	54	110	55
Private Car	60	20	78	26	48	24
Other (walk, bicycle)	6	2	--	--	--	--
Varies	24	8	12	4	2	1
TOTAL	300	100	300	100	200	100

This was also true for residents of Maryland and Virginia.

Twenty percent of the District residents interviewed normally travel to work by private automobiles. During the alert, 13% of these residents used their automobiles. Of the 7% who changed their mode of travel, only 2% attribute this change to the air pollution episode. Five percent gave other reasons, including expensive parking or car not readily available, i.e., in use by another member of the family.

The 1970 Census reports that 36% of D.C. residents commute by bus

compared to a 15% total for the metropolitan area. There was a slight decrease in the use of individual cars by Maryland and Virginia commuters, 6% in both cases (Tables 3 & 4). Four percent of the Virginia residents remained at home during the alert which may account in part for this decrease. Fifty percent of those who remained at home said they did so because of various reasons; "the hot weather", "the air pollution", or "I did not feel well", or "vacation". Of the eighteen District residents who remained at home during the alert only two gave "air pollution" as a reason.

Recognizing that a good public transportation system is a key element in the Regional Air Quality Control Plan for the Washington metropolitan region, we were interested in the views of residents regarding the metropolitan transportation system. Table 5 summarizes the responses to the questions about the Washington Metropolitan Transit Authority. Fifty-four percent of the D.C. respondents (162 persons) felt that buses were "too crowded" during the rush hour and that the waiting period was "too long". Ten percent of those expressing this opinion identified their residence as "upper Northwest"; 13% lived in Southeast, and 30% lived in Northeast Washington.

Fifty-five percent of Maryland residents, and 60% of the commuters and shoppers residing in Virginia said that their neighborhood was not "adequately" served by public transportation and that "catching a bus is inconvenient" for them. Twenty-six percent of the D.C. residents gave a similar response. Four percent of D.C. residents thought that the present bus system is insufficient without a complementing subway system. Two percent in Maryland shared this view while only 1% of the northern Virginia interviewees agreed.

Discussion & Conclusion

One of the most pervasive, widely accepted and least analyzed themes in the entire literature on air pollution concerns the asserted desirability, and even necessity, for citizen involvement at community levels in programs to control the quality of air resources.

Several statements by students of air pollution control^{5,6} and the experience of state and local regulatory agencies corroborate the view that participation of an educated citizenry in air pollution control is probably more important than any other community problem.

Much more supporting evidence may be drawn from the annals of air pollution control activities in the United States where initiative of citizens' associations have been widely credited with cleaning up smoke in Cincinnati and St. Louis and the black smogs of Pittsburgh. In still other cases citizens' committees have served as continuous advisory bodies to governmental agencies concerned with air quality management. As early as 1946 a citizens' dust committee was formed in one small community and its efforts resulted in successful prosecution of a lawsuit against an offending cement company.⁷ The Clean Air Act of 1970 brought into sharper focus the need to restrict motor-vehicle travel (an individual activity) in many urban centers, and as William Stevens wrote in the New York Times (July 15, 1973) "There appears no doubt that many Americans are viewing this prospect with, at least, considerable skepticism and outright defiance."

The results of this study indicate a reluctance on the part of some citizens to change individual behavior (mode of travel) to improve environmental quality for even a short period of time. It is also evident that the mere announcement on radio and in the newspaper of an air pollution episode (alert stage) is not sufficient to motivate changes in habits, attitudes and behavior with regard to those factors which contribute to levels of pollution. This obviously raises the question of the ways in which present reality of air quality and future ideals of air resources management are involved in the community's perception of air pollution problems and the mode of responses to them. While public support for air pollution control regulations, in general and the recently developed "Regional Air Quality Implementation Plan for the District of Columbia" in particular, have been good, it would appear that there are variations in individual perceptions of

TABLE 4

Mode of Transportation During the Air Pollution Alert

QUESTION: How did you travel to work and shop during the alert?

RESPONSE:

Mode of Transportation	Place of Residence					
	D. C.		Maryland		Virginia	
	No.	%	No.	%	No.	%
Bus	165	55	60	20	40	20
Car Pool	78	26	180	60	116	58
Private Car	39	13	60	20	36	18
Other	--	--	--	--	--	--
Remained Home	18	6	--	--	8	4
TOTAL	300	100	300	100	200	100

TABLE 5

Attitudes Toward Transportation System

QUESTION: Attitudes toward public transportation (Metrobus)

RESPONSE:

	Place of Residence					
	D. C.		Maryland		Virginia	
	No.	%	No.	%	No.	%
Inconvenience of buses	78	26	165	55	120	60
Bus routes do not extend far enough into residential areas	48	16	90	30	48	24
Overcrowding	162	54	39	13	30	15
Existing system is insufficient	12	4	6	2	2	1
TOTAL	300	100	300	100	200	100

PUBLIC BEHAVIOR DURING AIR POLLUTION

PRICE AND WALKER

and commitment to values regarding the effective management of local air resources; especially if that management impinges on traditional habits, attitudes and behavior or life styles (in this case a free life-style based on the automobile). As one report⁸ indicated, "people who hate freeways are still willing to have them built and use them because they get to work faster than before."

Thus, additional research is needed to discover how different values about air quality are manifested and ordered among different segments of the population. How do they vary with socioeconomic orientation and ecological sensitivity? In fact, it may even be appropriate to continuously re-examine the epidemiological basis for the current national ambient air quality standards.

This re-examination will obviously raise two fundamentally related questions. First, is our current scientific knowledge of the possible health effects of air pollution sufficient to stimulate community support for air resources management programs? Second, is the relationship of dose and response known for the major pollutants; and, if so, can it be clearly translated into effective plans for the prevention and control of mobile and stationary sources of atmospheric pollution, a plan which can gain total community understanding and support?

These considerations cannot and should not be overlooked by the health and medical community, especially health systems planners, or regulatory agencies because they are essential not only in the appropriate design of community health service programs such as air pollution control, but are critical in predicting community reactions to such services. Indeed, these reactions may determine success or failure of public and private efforts to improve air quality or the implementa-

tion of related comprehensive community health policies and programs which attempt to prevent the occurrence and progression of acute and chronic diseases.

References

1. FIRKET, J.: Fog Along the Meuse Valley. *Trans Faraday Soc.* 1936, 32: 1192-1197.
2. FIRKET, J.: Sur Les Causes des Accident Survenus dans la Valle de Decembre 1930. *Bull Aca Roy Med Belg* 1931, 11:683-793.
3. SHRENK, H. H., *et al*: Air Pollution in Donora, Pennsylvania. *Public Health Bull.* No. 306, Division of Industrial Hygiene, U.S. Public Service, Washington, D.C.
4. WILKENS, E.T.: Air Pollution and the London Fog of December, 1952. *Roy. Meterol Soc J.* 1954, 80:267-271.
5. *Proceedings*, National Conference on Air Pollution, Washington, D.C. Government Printing Office, 1958.
6. SCHUENEMAN, J. J.: Air Pollution Control Administration. *J. Air Pollution Control Assn.* 1962, 8:401-429.
7. MEDALIA, N. Z.: Citizen Participation on Environmental Action: The Case of Air Pollution Control. *AJPH* 1969, 59:1385-1391.
8. *Environmental Quality and Social Behavior—Strategies for Research*, National Academy of Sciences. Washington, D.C. 1973.

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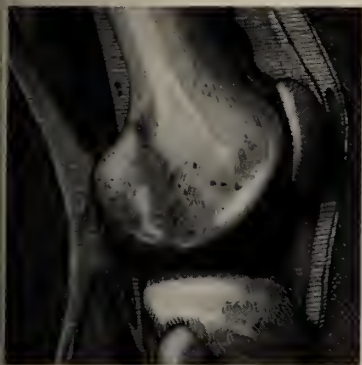
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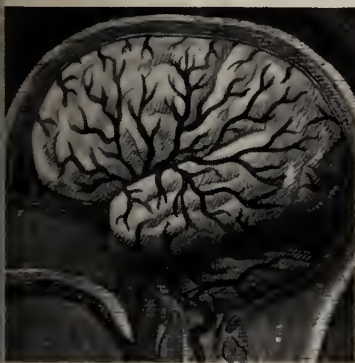
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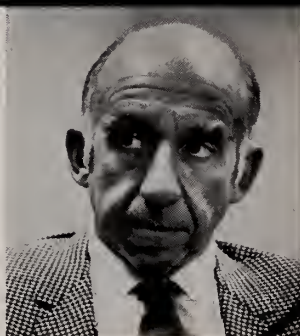
Family Physician's Perception

I think that most general practitioners in this area feel as I do about the detail man. Over the years I have gotten to know most of the men who visit me regularly and they in turn have become aware of my particular interests and the nature of my practice. They, therefore, limit their discussion as much as possible to the areas of interest to me. Since I usually see the same representative again in future visits, it is in his best interest to supply me with the most honest, factual, as well as up-to-date information about his products.



Dr. Willard Gobbell
Family Physician
Encino, California

Dr. Jeremiah Stamler
Chairman
Department of Community
Health and Preventive
Medicine, and Dingman
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The Positive Influence

My contact with representatives and salesmen of the pharmaceutical industry is the type of contact that people in a medical center, research people, and academic people have and that's in all likelihood on a somewhat different level from that of the practicing physician.

Let me touch on how I personally perceive the role of the sales representative. These men reach large numbers of health professionals. Thus they could be—and at times actually are—disseminators of useful information. They could consistently serve a real educational function in their ability to discuss their products.

At present they do distribute printed material, brochures and pamphlets—some of it scientifically sound and therefore truly useful—as well as some excellent films produced by the pharmaceutical industry. When they function in this

Opinion
&
Dialogue

Is He a Source of Information?

Yes, with certain reservations. The average sales representative has a great fund of information about the drug products he is responsible for. He is usually able to answer most questions fully and intelligently. He can also supply reprints of articles that contain a great deal of information. Here, too, I exercise some caution. I usually accept most of the statements and opinions that I find in the papers and studies which come from the larger teaching facilities. It goes without saying that a physician should also rely on other sources for his information on pharmacology.

Training of Sales Representatives

Ideally, a candidate for the position as a sales representative of a pharmaceutical company should be a graduate pharmacist who has a questioning mind. I don't think this is possible in every case, and so it becomes the responsibility

of the pharmaceutical company to train these individuals comprehensively. It is of very great importance that the detail man's knowledge of the product he represents be constantly reviewed as well as up-dated. This phase of the sales representative's education should be a major responsibility of the medical department of the pharmaceutical company.

I am certain that most of these companies take special care to give their detail men a great deal of information about the products they produce—information about indications, contraindications, side effects and precautions. Yet, although most of the detail men are well informed, some, unfortunately, are not. It might be helpful if sales representatives were reassessed every few years to determine whether or not they are able to fulfill their important function. Incidentally, I feel the same way about periodic assessments of everyone

in the health care field, whether they be general practitioners, surgeons or salesmen.

Value of Sampling

I personally am in favor of limited sampling. I do not use sampling in order to perform clinical testing of a drug. I feel that drug testing should rightly be left to the pharmacology researcher and to the large teaching institutions where such testing can be done in a controlled environment.

I do not use samples as a "starter dose" for my patients. I do, however, find samples of drugs to be of value in that they permit me to see what the particular medication looks like. I get to see the various forms of the particular medication at first hand, and if it is in a liquid form I take the time to taste it. In that way I am able to give my patients more complete information about the particular medications that I prescribe for them.

capacity they are indeed useful; particularly in the fact that they disseminate broadly based educational material and serve not just as "pushers" of their drugs.

The Other Side of the Coin

Obviously, the pharmaceutical companies are not producing all this material as a labor of love—they are in the business of selling products for profit. In this regard the ambitious and improperly motivated sales representative can exert a negative influence on the practicing physician, both by presenting a one-sided picture of his product, and by encouraging the practitioner to depend too heavily on drugs for his total therapy. In these ways, the salesman has often distorted objective reality and undermined his potential role as an educator.

The Industry Responsibility

Since the detail man must be an information resource as well as a representative of his particular pharmaceutical company, he should be carefully selected and

thoroughly trained. That training, perforce, must be an ongoing one. There must be a continuing battle within and with the pharmaceutical industry for high quality not only in the selection and training of its sales representatives, but also in the development of all of its promotional and educational material.

The industry must be ready to accept constructive as well as corrective criticism from experts in the field and consumer spokesmen, and be willing to accept independent peer review. The better educated and prepared the salesman is, the more medically accurate his materials, the better off the pharmaceutical industry, health professionals and the public—i.e., the patients—will be.

Physician Responsibility

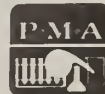
The practicing physician is in constant need of up-dated information on therapeutics, including drugs. He should and does make use of drug information and answers to specific questions supplied by the pharmaceutical representative. However, that informa-

tion must not be his main source of continuing education. The practitioner must keep up with what is current by making use of scientific journals, refresher courses, and information received at scientific meetings.

The practicing physician not only has the right, but has the responsibility to demand that the pharmaceutical company and its representatives supply a high level of valid and useful information. I feel certain that if such a high level is demanded by the physician as well as the public, this demand will be met by an alert and concerned pharmaceutical industry.

From my experience, my impression is that sectors of the pharmaceutical industry are indeed ethical. I challenge the industry as a whole to live up to that word in its finest sense.

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INDEX

Pagination

<i>Pages</i>	<i>No.</i>	<i>Month</i>	<i>Pages</i>	<i>No.</i>	<i>Month</i>
1-49	1	January	319-368	7	July
50-120	2	February	369-412	8	August
121-162	3	March	413-472	9	September
163-208	4	April	473-535	10	October
209-266	5	May	536-587	11	November
267-318	6	June	588-628	12	December

President's Message—Irving Burka, M.D. (p. 1 throughout year)

January—Phrases From A Pensive President
 February—The AMA-Who Needs It? We Do!
 March—Medical Records
 April—The News Media and the Doctor "News—the Manna of
 the Day"
 May—Health, Welfare and Politics
 June—What Price Health?

July—Midsummer Daydreaming
 August—The Rx
 September—A Doctors' Union?
 October—PSRO—Bane or Boon?
 November—An Indignity
 December—Reflections of an Outgoing President

Editorials

January
 On the Subject of Interdependence (Jay R. Shapiro), 3
 Well Done, Dr. Thomas W. Mattingly (Raymond Scalettar), 3
February
 Psychiatry: Fragmented Specialty? (Zigmond Lebensohn), 3
 Anesthesiologists and Acupuncture (M.L.B.), 4
 Utilization and Fee Review (Jerome Canter), 5
March
 The Mounting Storm-Drugs (James G. Kane, Jr.), 3

Electrocardiogram Comparisons (Juan B. Calatayud), 4
April
 What the Government Bestows the Government Can Take
 Away (Louis Gillespie), 3
 Hasty Health (Paul Schlein), 4
 Denial of Insurance Benefits (Robert W. Langevin), 5
 What Has Happened to the fine Art of Consultation? (John
 M. Keshishian), 6
May
 untitled (Raymond T. Holden), 3

1973 INDEX

June

In Defense of Electroshock Therapy (Zigmond M. Lebensohn), 3

July

The Irrelevance to Truth of Majority Opinion and Authority (W. Montague Cobb), 3

A Conceptual Model for Rehabilitation (John Naughton & Fred Leonard), 6

August

Psychiatry: Art and Business (William G. Tompkins), 2

An Alternate Method of Treating Chronic Fissures-in-Ano (John J. O'Connor), 3

September

The Georgetown University Medical Center Issue (John J. Canary), 2

October

none

November

Walter Reed Army Medical Center (Robert Bernstein), 3

December

The Treatment of Breast Cancer (Chandler Smith), 3

Scientific Authors

Aaronson, Charles M., 176
Absolon, Karel B., 11
Adkins, Paul C., 599
Agostini, Juan C., 11
Albert, Solomon N., 1, 11
Aposos, James, 486
Bacos, James M., 129
Barton, William I., 287
Basu, Asit P., 11
Bedynek, Julius L., 559
Bergevin, Patrick R., 545
Berkeley, Mary J., 229
Bernstein, R. B., 480
Bhatia, Chandrakant, 51
Bickham, Charles E., Jr., 217
Blackwell, Frances, 291
Blanck, Ronald R., 559
Blundell, George P., 222
Boivin, Michael R., 129
Boone, J. T., 480
Branson, Corolynne G., 390
Brouillard, Robert P., 563
Burman, Kenneth D., 541
Burns, Willard A., 65
Caceres, Cesar A., 234
Cammerer, Richard C., 553
Canary, John J., 429
Canter, Jerome W., 14
Chretien, Jane H., 375
Cohen, Lawrence S., 132
Collin, Daniel B., 556
Cornwell, Edward E., 291
Corso, Paul J., 599
Cox, Philip A., 182
Cruz, Iluminado, 185
Danovitch, Stuart H., 51
Deguzman, Vicente C., 165, 267
Dillard, Martin G., 185
Dobbins, William O. 111, 319, 331
DuPont, Robert L., 323
Eckelman, William C., 1

Epstein, Barry H., 6
Esswein, John C., 375
Farhoudi, Habib O., 390
Garagusi, Vincent F., 375
Geelhoed, Glenn W., 599
Geerken, Reynaldo G., 556
Gerstein, Kathleen Kretzmer, 55
Giordano, Joseph M., 599
Goldsweig, Howard, 334
Gordon, Theodore J., 498
Guha, Atin, 327
Hayman, Charles R., 229
Heath, Hunter III, 545
Hecker, Robert C., 180
Heit, Howard, 331
Herson, J., 378
Heshmat, M. Y., 378
Higgins, George A., 277
Hochberg, Howard M., 234
Homayouni, Masud, 182, 291
Hosten, Adrian O., 185
Joseph, William L., 595, 599
Kadar, Attila T., 65
Kleh, Jack, 385
Kovi, J., 378
Kozloff, Louis, 595
Kramer, Norman, 327
Krees, Stephen V., 4
Kushner, David H., 603
Ladas, Gregory John, 273
Law, Ivan P., 548
Lee, James B., 419
Lessin, Lawrence, 334
Lieberman, Martin S., 319
Lin, Royce, 327
Lyons, William S., 165, 173, 225, 267
Markel, William M., 495
Martin, Arline L. A., 423
Martin, Malcolm M., 423
Matthews, Mary J., 277
Mazer, Steven F., 490

Meek, Hibbs S., 229
Mendelson, Sander H., 17
Meyersburg, Herman A., 385
Mody, Vinod R., 390
Moore, Ralph W., 121
Morowitz, David A., 6
Motomiya, Takeshi, 280
Nicklas, Richard A., 59
Niles, R., 378
O'Connell, J. M. Brian, 277
Pan, John, 603
Parrish, Alvin E., 327
Pasternack, Stefan A., 369
Peabody, Joseph W., Jr., 165, 267
Perl, Stanley, 173
Piemme, Thomas E., 323
Piscatelli, R. L., 480
Pittman, James A., Jr., 435
Raposo, Carlos, 327
Reba, Richard C., 1
Reitz, R. E., 480
Robbins, Guy F., 495
Robbins, Paul R., 385
Rogers, Jerry B., 14
Rowinski, Glenn, 55
Sabatini, Domenic E., 124
Schechter, Geraldine, 334
Schliffman, Alan, 339
Schroeder, Steven A., 339
Seremetis, Michael G., 165, 225, 267
Shalhoub, Robert J., 277
Shapiro, Jay R., 17
Siebelt, Barbara, 234
Singh, Baikunth K., 280
Singleton, Peter T., 559
Smith, Ray B., 55
Sode, Jonas, 136
Standard, Raymond L., 229
Thompson, Anne, 327
Thompson, William F., 62
Tidball, Charles S., 473

Ullman, Kenneth, 121
 Uy, Antonio, 277
 Vance, Vernon K., 419
 Venkatesan, Ranganathan, 327
 Vieweg, Walter V. R., 136, 480

Walker, Bailus, 498
 Wallach, Howard W., 17
 Warkel, Rapheal L., 541
 Wartofsky, Leonard, 541
 Weinstein, R. L., 480

Wener, Louis, 173
 Werthmann, Milton W., Jr., 4
 Whiplinger, Carl, 334
 Wilbur, Ronald D., 605
 Wilson, Robert, 327

Scientific Articles

Acute Pancreatitis with Extensive Peripheral Fat Necrosis Simulating Erythema Nodosum and Abdominal Cyst (Dobins, Liberman), 319

Adrenal Insufficiency Resulting from Metastasis of Non-functioning Adrenocortical Carcinoma (Heath, Bergevin), 545

The American Connection: Handguns and Homicide (Pasternack), 369

Application of Thermography in Peripheral Vascular Disease (Singh, Motomiya), 280

Automatic Ultrasonic Measurement of Brachial and Popliteal Blood Pressures for Health Testing (Caceres, Sibelt, Hochberg), 234

Azotemic Malignant Hypertension: Clinical Course and Surgical with Vigorous Anti-hypertensive Regimen and Intermittent Dialysis (Cruz, Dillard, Hosten), 185

Carcinoembryonic Antigen (CEA): A Review and Current Status (Blundell), 222

Cardiorespiratory Complications of Intravenous Drug Abuse (Blanck, Singleton, Bedynek), 559

A Case of Severe Varicella in an Adult (Farhoudi, Mody, Branson), 390

Choledochoduodenal Fistula: A Rare Complication of Duodenal Ulcer, Report of Three Cases (Bickham), 217

Complications of Cardiac Pacemakers (Seremetis, Deguzman, Lyons, Peabody), 165

Complications of Therapeutic Abortion Utilizing Intra-amniotic Hypertonic Saline (Pan, Kushner), 603

Congenital Bronchoesophageal Fistula in the Adult, Report of Three New Cases (Lyons, Seremetis), 225

Cystic Dilatation of the Common Bile Duct in Adults (Kozloff, Joseph), 595

Detection of Aspirin Sensitivity by Pulmonary Function Tests (Nicklas), 59

Doctors, Digits and Disks (Tidball), 473

The Doctor's Thorn (Moore, Ullman), 121

Dysphagia Lusoria: A Forgotten Entity? (Cammerer), 553

An Epidemiologic Study of Gonorrhea and Cancer of the Prostate Gland (Heshmat, Herson, Kovi, Niles), 378

Estimation of the Number of Narcotic Addicts in an Urban Area (DuPont, Piemme), 323

Evaluation of Biologic Availability of Digoxin Preparations Available to a Naval Hospital (Vieweg, Sode), 136

Evidence of Chronopathology in Alcoholism (Smith, Rowinski, Gerstein), 55

Extraction of Catheter Fragment from the Pulmonary Bed by Non-Surgical Catheter Technique (Bacos, Boivin), 129

Gastrin: A Review (Bhatia, Danovitch), 51

Giardiasis in Young Adults (Chretien, Esswein, Garagusi), 375

Hepatitis Virus B. Infection in an Alcoholic with Cirrhosis (Heit, Dobbins), 331

Hypercalcemia During the Diuretic Phase of Acute Renal Failure (Wilson, Raposo, Venkatesan, Lin, Thompson, Guha, Kramer, Parrish), 327

Hyperfunctioning Thyroid Nodules that Become "Cold" (Burman, Warkel, Wartofsky), 541

Hypertension and Human Renal Prostaglandins (Vance, Lee), 419

Hypohidrotic Ectodermal Dysplasia; An Unusual Presentation (Wilbur), 605

Ineffective Erythropoiesis (Brouillard), 563

The Influence of Medical School on Selection of Career Specialties (Schroeder, Schlifman), 339

Intractable Ascites During Maintenance Hemodialysis (Uhl, Shalhoub, O'Connell, Matthews, Higgins), 277

Intra-Gastric Rupture of a Splenic Artery Aneurysm (Rogers, Canter), 14

Management of Uncontrolled Thyroid Carcinoma (Sabatini), 124

Medroxyprogesterone Acetate (Provera^R) Therapy in Acromegaly Associated with Heart Disease (Wallach, Shapiro, Mendelson), 17

Membrane Lung Support in Acute Respiratory Insufficiency (Joseph, Corso, Geelhoed, Giordano, Adkins), 599

Metastases in Bone Marrow and Pancytopenia from Carcinoma of the Lung (Report of a patient and review of the literature) (Law), 548

^{99m}Tc Sodium Pertechnetate Scanning of the Abdomen, A Valuable Tool for Detection of Meckel's Diverticulum (Gerken, Collin), 556

Obesity—A Form of Malnutrition (Martin, Martin), 423

Perforations and Ruptures of the Esophagus (Lyons, Seremetis, Deguzman, Peabody), 267

Peutz-Jeghers Syndrome Case Report (Cornwell, Homayouni, Blackwell), 291

The Postmastectomy Lymphedematous Arm (Robbins, Markel), 495

Postoperative Abdominal Wall Necrosis (Aaronson), 176

Primary Carcinoma of the Vagina, Case Report and Review of the Literature (Hecker), 180

Provision of Emergency Health Care at a Rock Festival (Haymon, Standard, Meek, Berkeley), 229

Pseudoaneurysm After Angiography (Perl, Wener, Lyons), 173

Psychiatric Aspects of Addison's Disease: Report of a Case

1973 INDEX

- (Thompson), 62
 Psychological Problems in the Care of the Institutionalized Aged: A Look at D.C. Village (Robbins, Kleh, Meyersburg), 385
 Quantitative Excretion of Senokot in Human Breast Milk (Werthmann, Krees), 4
 The Relationship of Hepatitis Associated Antigen (Australia Antigen) and Chronic Active Hepatitis—Review of Current Literature (Mazer), 490
 Review of the Medical Management of Acute Variceal Bleeding from the Esophagus (Aposos), 486
 Severe Multisystem Allergic Reaction to Sulfisoxazole (Goldswieg, Whiplinger, Schechter, Lessin), 334
 Some Thoughts on the Medical Management of Renal Stones (Canary), 429
 Spectrum of Bowel Disease Associated with Use of Oral Contraceptives (Morowitz, Epstein), 6
 Sporotrichosis of the Thumb. A Case Report (Cox, Homa-youni), 182
 A Statistical Study of Infants Born with Withdrawal Symptoms in the District of Columbia (Barton), 287
 Tc-99m Labeled Red Blood Cells: A New Radiopharmaceutical for the Determination of Total Blood Volume and Blood Pool Scanning (Reba, Eckelman, Albert), 1
 Temporal Arteritis: A Review of the Washington Hospital Center Experience with Comparison of the Literature (Ladas), 273
 Total Body Asanguineous Hypothermic Perfusion and Blood Volume Exchange in Dogs (Agostini, Basu, Albert, Abso-lon), 11
 Treatment of Cardiogenic Shock (Cohen), 132
 Unusual Metastases from a Transitional-Cell Carcinoma of the Renal Pelvis and Ureter (Burns, Kadar, 65
 Varieties of Hypothyroidism (Pittman), 435
 Viral Hepatitis: Metabolic Studies During Acute and Con-valescent Phase (Vieweg, Piscatelli, Boone, Reitz, Bern-stein, Weinstein), 480

Book Reviews—Authors

- | | | |
|--------------------------------------|--------------------------------|--------------------------------|
| Absolon, Karel B., 256 | Kramer, Norman C., 624 | Schisgall, Richard M., 251 |
| Albert, S. N., 464 | Kushner, Edward I., 409 | Seltzer, Alvin, 151 |
| Alpert, Louis K., 464 | Larosa, John C., 246 | Sherer, Max G., 108 |
| Augustin, Gunter J., 201 | Lawrinson, Walter E., 245 | Shnider, Bruce I., 626 |
| Avery, Gordon B., 45 | Lee, Allan E., 107 | Shugoll, Gerald I., 529 |
| Boinis, George A., 303 | Lindgren, Keith M., 586 | Silby, Howard M., 624 |
| Brown, Thomas McPherson, 367 | Lindsay, Joseph Jr., 38 | Silva, Carlos A., 106 |
| Chap, Eugene J., 205 | Malloy, Bernard Mathis, 251 | Silverberg, Stanley M., 303 |
| Curtin, James A., 625 | Manchester, Benjamin, 367, 530 | Smith, Chandler, 584 |
| Datinsky, David, 625 | Margileth, Andrew M., 150 | Sokoloff, Leon, 205 |
| deLeon, Antonio C., Jr. 49, 108, 584 | Marland, Albert E. Jr., 155 | Stewart, Steele F. Jr., 105 |
| Ein, Daniel, 156 | Harold S., 149 | Stubenbord, John, 45, 315, 463 |
| Elgart, Mervyn L., 204 | Moore, W. Tabb., 107 | Suraci, Alfred J., 103 |
| Fitzgerald, James E., 106 | Moran, Robert E. Jr., 37, 201 | Thomas, Martin A., 245 |
| Frey, Thomas, 41 | Noble, Raymon A., 251 | Thompson, Anne M., 583 |
| Friedberg, Felix, 529 | Pappas, Stephen S., 315 | Tompkins, W. G., 623 |
| Ginsberg, Allen L., 583 | Parrish, Alvin E., 367 | Tralka, George A., 105 |
| Goodman, Nelson G., 310 | Peele, Roger, 153 | Vivino, A. Earl, 154, 259 |
| Grand, Bernard, 303 | Periman, Phillip, 531 | Weintraub, Alan M., 205 |
| Haas, Stephen S., 309 | Perkins, John C., 38 | Werthmann, Milton W. Jr., 409 |
| Kenrick, Margaret, 410 | Putnam, Lawrence E., 204 | Wilner, Elliot C., 463 |
| Kleinerman, Morris, 584 | Ruskin, Arthur, 43 | Wilson, Norman L., 104 |
| Knapp, Deanne, 43 | Saidman, Aaron G., 154 | Wolfe, Martin S., 585 |
| Korengold, Marvin C., 105 | | |

Book Reviews

- | | |
|--|--|
| An ABC of Endocrinology. K.J. Catt, M.D. (Sherer), 108 | Air Pollution and Respiratory Disease. W.W. Holland, Editor. |
| An ABC of Medical Genetics. C.O. Carter, F.R.C.P. (Stewart), 105 | (Seltzer), 150 |
| Acute Inflammation. J. V. Hurley, M.D. (Stubenbord), 463 | Alcohol and Health. Report from the Secretary of HEW. (Silby), 624 |

- Applications of Proteolytic Enzymes to Protein Structure Studies. Elmer Mihalyi, M.D., Ph.D. (Vivino), 154
- Artificial Organs and Cardiopulmonary Support Systems. Felix T. Rapaport and John P. Merrill, Editors. (Absolon), 256
- Auxiliaries in Health Care, N.R.E. Fendall. (Wolfe), 585
- Cardiac Hypertrophy. Norman R. Alpert, Editor. (Manchester), 368
- Clinical Concepts of Infectious Diseases. Leighton E. Cluff, M.D. and Joseph E. Johnson, III, M.D., Editors. (Perkins), 38
- Clinical Nephrology. Solomon Papper. (Parrish), 367
- Common Problems in Office Practice. Robert B. Taylor, M.D. (Goodman), 310
- Congenital Abnormalities in Infancy. A.P. Norman, Editor. (Avery), 45
- A Consumer's Dictionary of Food Additives. Ruth Winter. (Saidman), 154
- Current Diagnosis and Treatment 1973. Marcus A. Krupp and Milton J. Chatton. (Boinis), 303
- Current Pediatric Diagnosis and Treatment. Henry Kempe, M.D., Henry K. Silver, M.D. and Donough O'Grien, M.D. (Margileth), 149
- Current Research in Oncology. C.B. Anfinsen, Michael Potter and Allan N. Schechter, Editors. (Shnider), 626
- Current Therapy-1972. Howard R. Conn, M.D. (Fitzgerald), 106
- Dermal Pathology. James H. Graham, M.D., Waine C. Johnson, M.D. and Elson B. Helwig, M.D., Editors. (Elgart), 204
- Differential Diagnosis. The Interpretation of Clinical Evidence. A. McGehee Harvey, M.D. and James Bordley, III, M.D. (Putnam), 204
- Drugs and the Public. Norman E. Zinberg, M.D. and John A. Robertson. (Knapp, Ruskin), 43
- Early Care of the Injured Patient. Comm. on Trauma, Am. College of Surgeons. (Silva), 106
- Emergency Room Diary. Theodore Isaac Rubin, M.D. (Noble), 251
- Essentials of Artificial Ventilation of the Lungs. A.R. Hunter. (Albert), 464
- Essentials of Cardiac Arrhythmias. Diagnosis and Management. Samuel Bellet, M.D. (Weintraub), 208
- Essentials of Roentgen Interpretation. Lester W. Paul, M.D. and John H. Juhl, M.D. (Augustin), 201
- The First Congress of the International Strabismological Association. Peter Fells, M.A., M.B. (Frey), 41
- Frontiers in Comparative Medicine, Vol. 1, No. 1. W.I.B. Beveridge. (Curtin), 625
- Functional Aids for the Multiply Handicapped. Isabel P. Robinault, Ph.D., Editor. (Kenrick), 410
- The Genetic, Metabolic and Developmental Aspects of Mental Retardation. Robert R. Murray, Jr., M.D. and Pearl Lockhart Rosser, M.D., Editors. (Chap), 205
- Handbook of Medical Treatment. Milton J. Chatton, M.D., Editor. (Marland), 155
- A Handicapped Child in the Family. Verda Heisler, Ph.D. (Tompkins), 623
- Heart Block, Richard S. Cosby and Michael Bilitch. (Lindsay), 38
- Hematology. William J. Williams, Ernest Beutler, Allan J. Erslev and R. Wayne Rundles. (Mirsky), 149
- Hemodialysis. Principles and Practice. George L. Bailey, M.D., Editor. (Thompson), 583
- Hereditary Retinal and Choroidal Diseases. Alex E. Krill, M.D. (Pappas), 315
- Homeopathy in America. Martin Kaufman. (Stubenbord), 45
- The Human Spine in Health and Disease. George Schmorl and Herbert Junghanns. (Sokoloff), 205
- Immunology, Immunopathology and Immunity. Stewart Sell. (Ein), 156
- In a Darkness. James A. Wechsler. (Moran), 37
- Justifying Violence: Attitudes of American Men. Blumenthal, Kahn, Andrews, and Head. (Kushner), 409
- Laboratory Tests in Diagnosis and Investigation of Endocrine Function. Roberto F. Escamilla. (Moore), 107
- The Language of Fractures. Robert J. Schultz, M.D. (Haas), 309
- Lipids, Malnutrition and the Developing Brain. A Ciba Foundation Symposium. (Vivino), 259
- The Making of a Psychiatrist. David S. Viscott, M.D. (Moran), 201
- Management and Treatment of Tropical Diseases. B.G. Maegraith and H.M. Gilles, Editors. (Tralka), 105
- The Management of Neonates and Infants with Congenital Heart Disease. Donal M. Billig, M.D. and Marshall B. Kreidberg, M.D. (deLeon), 584
- The Medical Garden. Geoffrey Marks and William K. Beatty. (Ruskin), 465
- Medicine and Ethnology. Erwin H. Ackerknecht. (Wilson), 104
- The New Hospital Psychiatry. Gene N. Abroms and Norman S. Greenfield, Editors. (Peele), 153
- Non-Human Primates and Medical Research. Geoffrey H. Bourne, Editor. (Kramer), 624
- The Pathogenesis of Atherosclerosis. Robert W. Wissler and Jack C. Gerr, Editors. (Larosa), 246
- Pathogenic Mycoplasmas. A Ciba Foundation Symposium. (Brown), 367
- Pathophysiology of Gestation. Nicholas S. Assali and Charles R. Brinkman. (Werthmann), 409
- Peptide Transport in Bacteria and Mammalian Gut. A Ciba Foundation Symposium. (Vivino), 259
- Photomicrography. Douglas Lawson. (Smith), 584
- Physiology, Emotion and Psychosomatic Illness. A Ciba Foundation Symposium. (Kleinerman), 584
- Plastic and Reconstructive Surgery. Hans May, M.D., F.A.C.S. (Suraci), 103
- Practical Management of the Elderly. W. Ferguson Anderson. (Lee), 107
- Principles of Clinical Electrocardiography. M.J. Goldman, M.D. (Shugoll), 529
- Progress in Clinical Pathology, Vol. IV. Mario Stefanini, Editor. (Lawrinson), 245

1973 INDEX

- Progress in Liver Diseases, Vol. 4. H. Popper and F. Schaffner, Editors. (Ginsberg), 583
- Progress in Neurology and Psychiatry, Vol. 27. E.A. Spiegel, M.D. (Satinsky), 625
- The Psychoanalytic Study of Society. Warner Muensterberger and Aaron Esman, Editors. (Malloy), 251
- Pulmonary Reactions to Coal Dust. A Review of U.S. Experience. Marcus M. Key, Lorin E. Kerr and Merle Bundy, Editors. (Grand), 303
- Radiologic Examination of the Urinary Tract. Howard M. Pollack, M.D. (Thomas), 245
- Review of Physiological Chemistry. H.A. Harper. (Friedberg), 529
- Supportive Care of the Surgical Patient. William M. Stahl, M.D. (Stubenbord), 315
- Surgical Pediatrics. Stephen L. Gans, M.D., Editor. (Schisgall), 251
- Textbook of Electrocardiography. David Littmann, M.D. (deLeon), 49
- Tissue Typing Techniques. Heather M. Dick and W. Barry Crichton. (Periman), 531
- Understanding Cancer. Bryan N. Brooke. (Alpert), 464
- Vectorcardiography. Alberto Benchimol, M.D. (Lindgren), 585
- Vectorcardiography in Congenital Heart Disease. R. Curtis Ellison, M.D. and Norma J. Restieaux, M.B., CH.B. (deLeon), 108
- Wolff's Headache and Other Head Pain. Revised by Donald J. Dalessio. (Korengold), 105
- Your Brain and Nerve. J. Lawrence Pool, M.D. (Wilner), 463

Special Articles—Authors

- | | |
|--------------------------|--------------------------|
| Cobb, W. Montague, 189 | Rucker, T. Donald, 609 |
| Gordon, Theodore J., 498 | Walker, Bailus, 498 |
| Kaplan, Hyman M., 566 | Ward, George W. Jr., 566 |
| Keshishian, John M., 294 | |

Special Articles

- | | |
|--|---|
| Are Women's Fashions Necessary? (Cobb), 189 | Economic Aspects of Drug Over Use (Rucker), 609 |
| Community Health Aspects of Water Pollution Problems (Walker, Gordon), 498 | F-Stop, Anyone? (Keshishian), 294 |
| | New Concepts in Asthma (Kaplan, Ward), 566 |

General

- | | |
|--|---|
| Adolescence and Preadolescence Committee, 579 | Medico- Legal Report |
| AMA Council Statement on Venereal Diseases, 3 | Liability for Transfusions of "Bad" Blood (Cass), 27 |
| Annual Business Meeting, 1972, 77 | Surgeon's Liability for Nurse's Negligence-The "Lent Servant" (MacDonald), 97 |
| Burka, Irving, President of the Medical Society of D.C., biography, 24 | Membership Committee Report, 619 |
| Colon- Rectal Cancer, Cancer Quiz, 523 | Report of the Delegates to the AMA Clinical Convention, John J. Hughes, M.D. and C. Willard Camalier, Jr., M.D. |
| ECG Problems (Montgomery), 175, 233, 272, 322, 384, 459, 497, 558, 598 | Smith, Robert B. W., New Associate Editor, <i>The Medical Annals of the District of Columbia</i> , 31 |
| From the Editors, Raymond Scalettar, M.D., Editor and Robert B. W. Smith, M.D. Associate Editor, 345 | The View Box (Augustin), 16, 86, 101, 145, 172, 221, 317, 350, 396, 422, 519, 552, 602 |
| Howard E. Ticktin Fund, 522 | |
| Medical Society Officers and Committees for 1973. 71 | |

Membership

- | | | |
|--------------------------|----------------------------|--------------------------|
| <i>Active</i> | Barry, Kevin G., 581 | Callender, Clive O., 581 |
| Adams, George L., 241 | Baselga, Jose Luis, 101 | Callender, Wilbur, 461 |
| Altstatt, Alice, 197 | Beale, Mary G., 621 | Cates, Charles H., 407 |
| Anderson, Ronald L., 297 | Beaumont-Hinds, Ilnes, 621 | Charles, Aloysius, 581 |
| Arora, Surinder, 407 | Berry, H. Lee, 101 | Chen, Cheng-Nan, 581 |
| Auster, Rosalie, 581 | Billig, Nathan, 461 | Cochrane, William, 197 |
| Bagalkotar, Balwant, 355 | Block, Jerome, 621 | Diamond, Louis, 241 |
| Barnes, Boisey O., 197 | Briscoe, William C., 197 | Dickey, Robert P., 355 |

- Dixon, Marden G., 355
 Doyle, Brian B., 581
 Ecker, Sidney, 621
 Edelson, Richard N., 621
 Epps, Roselyn, 297
 Estampador, Nerita R., 461
 Ettenson, Stephen, 621
 Falk, Richard, 297
 Fam, Wadie, 621
 Ferris, Robert A., 581
 Fidler, Stuart M., 355
 Fleming, Edward S., 621
 Gee, Chester, 461
 Ginsberg, Allen, 621
 Giordano, Joseph, 355
 Gomez, Lucie, 621
 Greer, Douglas, 407
 Gunlock, Howard, 581
 Gupta, Suresh C., 101
 Hall, Macy G., 581
 Hamill, John R., 355
 Harper, Eugene J., 581
 Harvey, John C., 407
 Helfrich, George B., 581
 Herenda, Maria M., 101
 Herrera, Hector, 355
 Hwang, Tin-Chaw, 355
 Ibrahim, William S., 461
 Jackson, Aaron, 355
 Jerome, Marc A., 581
 Jweied, Ghassan, 621
 Kaftarian, Hayk L., 407
 Kearing, Leon R., 101
 Kim, Se Duck, 461
 Kioko, Gideon, 461
 Klug, Panpit, 355
 Knepshield, James, 241
 Koos, Wolfgang T., 101
 Kutzin, Alice L., 197
 Kwan, Alex, 407
 Lee, Chang G., 241
 Lee, Swang M., 355
 Lerum, Natividad, 621
 Lim, Lily, 581
 Limaye, Suresh, 621
 Lopez- Muniz, Raul, 297
 Marsh, Henry B., 461
 Massengale, Minda, 461
 Melluzo, Paul J., 197
 Melton, John W., 621
 Minor, Maureen N., 101
 Mody, Vibhakar J., 461
 Moretti, John F., 461
 Moyer, Paul R., 461
 Napoli, Louis, 461
 Neviaser, Thomas J., 621
 Noel, Patrick, 407
 Odenwald, Robert P., 297
 Panton, Linton, 101
 Passaretti, Michael, 461
 Payseur, Garnett S., 581
 Plotsky, Harold, 241
 Raiford, Roger, 581
 Rankin, Edward, 581
 Restifo, Mary D., 355
 Robins, Douglas, 581
 Rosing, Douglas R., 581
 Rothschild, Stanley, 581
 Santos, Roland, 407
 Schainker, Lawrence H., 101
 Schneider, Roy L., 407
 Schutt- Aine, Joseph, 581
 Schwartz, Arthur, 621
 Schwartz, Don E., 581
 Segal, Amiel, 461
 Shah, Ramakant, 621
 Shauer, Bruce A., 581
 Shaver, Benjamin A., 581
 Shea, David William, 581
 Shelby, Harold, 621
 Shim, Poong Sup, 461
 Sinai, Kavoos, 241
 Skopek, Henry A., 581
 Small, Allen, 461
 Smith, Donald R., 407
 Snow, Jerry A., 355
 Stroud, Franklin, 241
 Taylor, Jack B., 621
 Taylor, Kathryn E., 581
 Taylor, Stever J., 581
 Tuerk, Jonathan D., 461
 Turkus, Joan A., 101
 Turner, Donald C., 581
 Ugel, Arthur R., 101
 Uy, Antonio, 461
 Vanhorn, Eugene, 355
 Vincent, Arthur, 101
 Weintraub, William H., 461
 Weir, Roger L., 101
 Westura, Edwin E., 581
 Wolin, Steven J., 621
 Yu, Kou-Chen, 297
- Associate*
 Coyle, William R., 297
 Desai, Ramesh, 621
 Goldberg, Stephan R., 297
 Gottlieb, Sheldon K., 101
 Gulbrandsen, Jon A., 102
 Henry, Ismay, 297
 Jordan, Raymond, 241
 Kultchar, Elizabeth, 461
 Kunkel, Charles, 582
 Light, Jimmy, 582
- Lipton, Simon M., 102
 McCann, Robert J., 582
 Mercado, Manuel, 297
 Moir, George D., 358
 Mroczek, William J., 197
 Newman, Stephan, 358
 Nieman, Rolf, 358
 Oboler, Allen, 297
 Odyniec, Norman A., 582
 Pepper, Franklin, 358
 Pilet, Jean C., 461
 Rice, Donald T., 197
 Rigor, Rita, 358
 Solano, Jose, 241
 Yanowitch, Robert E., 407
- Resident-Intern*
 Adair, Luther B., 102
 Adolph, Joseph, 462
 Aird, Cecil, 197
 Barlee, Manat, 408
 Beauchamp, George, 197
 Bier, Charles, 621
 Bryant, William C., 197
 Cartaya, Oscar A., 102
 Christian, Cora L., 102
 Connell, Neville, 408
 Curfman, David, 621
 De La Pava, Daniel, 197
 Deluca, Francis N., 102
 Dillon, Owen C., 197
 Elliot, William, 197
 Gerald, Melvin D., 102
 Goo, Walter Y., 102
 Goyal, Suresh C., 102
 Harris, Denis, 622
 Kenny, Lawrence, 408
 Kim, Sae C., 241
 Kim, Sae-In, 102
 Korengold, George, 408
 Landau, Barry J., 241
 Lorenzo, Loreto, 197
 Loube, Julian, 462
 McBride, John C., 102
 Maya, Hector J., 102
 Miller, Jack M., 197
 Minus, Harold R., 102
 Nickerson, Marshall, 622
 Rivera, Alejandro, 462
 Schumer, Dennis R., 582
 Smith, Vernon C., 622
 Smokvina, Marija, 622
 Spevak, Michael, 462
 Starr, George S., 197
 Stoleru, Samuel, 102
 Stopak, Bernard, 462
 Ullman, Kenneth C., 102

1973 INDEX

Weinstock, Alan R., 297

Student

Aurecchia, Steven A., 102

Beyer, Alan H., 102

Buckler, Robert E., 102

Burka, Steven A., 102

Carroll, Michael P., 102

Chuy, Feliciano, 102

Dwyer, Sean M., 102

Goodwin, Robert S., 102

Madonia, Eugene, 241

Perakos, Peter G., 102

Perlman, Mark Lewis, 241

Phelps, John E., 102

Sanz, Luis E., 102

Shapiro, Dein M., 102

Shubert, Dennis L., 102

Stryker, Margaret, 462

Yoshikawa, James S., 102

Zimmerman, Brian, 102

Obituaries

Ayton, Leonidas A., 627

Baensch, Willy E., 117

Clements, James M., 261

Coe, Frederick O., 587

Comeau, Norman D., 366

Cooper, Robert U., 264

Craft, Robert H., 265

Day, John Ronald, Jr., 261

Donnally, Reaumur S., 264

Duus, Peter 411

Egan, Thomas A., 119

Enlows, Ella M. A., 535

Epstein, Jerome H., 535

Foxwell, Raymond K., 411

Gonder, Thomas A., 213

Greenberg, Arnold S., 266

Hageage, Charles C., 627

Hawfield, Clayton, 118

Holmes, Charles K., 318

Harvath, Frank S., 118

Johnson, John B., 161

Kachmarick, John, 117

Kalandros, Elisabeth K., 365

Katzenelbogen, Solomon, 119

Knop, Anna Catharine Q., 471

Laughling, Kenneth F., 213

Leake, James P., 264

Lenhoff, Charles D., 161

Mankin, Gilbert H., 264

Mead, Sterling V., 162

Nash, Emile C., 118

O'Donovan, Timothy F., 265

Price, Kline A., 265

Robinson, Murray M., 411

Schoenfeld, Herbert H., 587

Seckinger, Daniel L., 261

Smith, David O., 471

Ticktin, Howard E., 365

Washington, Daniel B., 471

Watson, Joseph H., 412

MEDICAL ANNALS OF THE DISTRICT OF COLUMBIA

VOLUME XLIII

INDEX

Pagination

<i>Pages</i>	<i>No.</i>	<i>Month</i>	<i>Pages</i>	<i>No.</i>	<i>Month</i>
1-55	1	January	339-385	7	July
56-105	2	February	386-433	8	August
106-173	3	March	434-488	9	September
174-230	4	April	489-532	10	October
231-283	5	May	533-586	11	November
284-338	6	June	587-622	12	December

President's Message—Clifton Gruver, M.D.
(p. 5 through June)

January—Individual Consideration
February—Communication
March—Smallpox Vaccination—Passing of an Era
April—On Giving
May—Some Thoughts About Education
June—Acupuncture

Editorials

January

Colonoscopic Evaluation of Inflammatory Disease
(John J. O'Connor), 6
Regarding State Medical Journals, Including Ours (Robert B.
W. Smith), 6
Society Publications (Roger F. Mecum), 7
February
The Dangerous Sex Offender (David A. Lanham), 6
March
Pulmonary Medicine (Harold M. Silver), 6
Anticoagulation I: The Clinical Use of Heparin (Lawrence E.
Pierce), 7

April

Medical Records (Alfred Baer), 6
Anticoagulation II: Anticoagulant Usage in Cerebrovascular
Disease (Richard Edelson), 7

May

Anticoagulation III: Anticoagulation and Acute Myocardial
Infarction "What the Big Boys Do" (James A. Bacos), 7

June

Anticoagulation IV: Preventing Thrombosis by Modifying
Platelet Behavior (Edward Adelson and Amiel Segal), 7

July

untitled (J. William Oberman), 5

1974 INDEX

Clindamycin (James A. Curtin), 7

August

National Exercise and Heart Disease Project (John Naughton, Jack Taylor, Patrick Gorman, and Jorge Rios), 5

Intermittent IPPB Treatments: Therapy in Search of an Indication (Philip Witorsch), 9

September

Evaluation of Penicillin Hypersensitivity (Halla Brown, and revised by Solomon Barr, Richard Nicklas, and Isaac Weiszer), 5

October

Embryo Transplant—Worthy Goal or Misconception (Richard

J. Falk), 5

November

Office Hemorrhoidectomy (Elastic Band Ligation) (John J. O'Connor), 7

Hepatitis and the Need for Reporting (D.C. Dept. of Human Resources), 8

Australia Antigen (HB_sAg) (Allen L. Ginsberg), 9

December

To the Editor (Tzu-Min Kao, M.D., Cheng-Nan Chen, M.D. and Fred Chin Chu, M.D.), 5

Scientific Authors

Abram, Harry S., 59

Abramson, David C., 63

Absolon, Karel B., 233, 237, 241, 245, 251, 543

Ali, Nayab, 401

Alpert, Hubert J., 69

Ammerman, Bruce J., 593

Avery, Gordon B., 359

Bacos, James A., 245, 251

Baker, Norman R., 257

Banks, Tazewell, 401

Bashour, Tali, 549

Bedynek, Jules, 4

Blackburn, Glenn, 349

Brody, Arnold G., 72

Bruner, Blackwell S., 359

Burns, Willard A., 389

Conte, R. S., 457

Conney, F. Donald, 193

Cromer, J. Keith, 497, 499

Cruz, Iluminado A., 597

Currie, John L., 18

D'Ambrosio, Umberto, 4

Daniels, David H., 4

Danovitch, Stuart H., 533, 549

DeLeon, Randolph, 241

Diaz, Mario H., 245, 285

Dibble, Robert, 72

Dillard, Martin G., 597

Dobbins, John, 666

Dobbins, William O. III, 533

Doromal, Noel M., 285, 451

Driggers, David A., 25

Dunbar, Burdett S., 107

DuPont, Robert L., 175

Eaton, Olga M., 120

Edwards, Maureen C., 349

Falk, Richard J., 493

Farhoudi, Habib O., 401

Fatehi, Nasrollah, 193

Fermaglich, Joseph, 587

Finnerty, Frank A. Jr., 437

Fletcher, Anne B., 349

Frankl, William S., 9

Freant, Lawrence J., 233

Frey, Thomas, 359

Friendly, David S., 359

Garro, Arnaldo, A., 237

Geelhoed, Glenn W., 307, 441

Gerber, Leon, 549

Goldman, Milton L., 549

Goldstein, Robert A., 115

Gorfinkel, H. Joel, 395

Green, Gerald I., 124

Greene, Mark H., 175

Haider, Riaz, 395

Hall, John E., 21

Heckman, Bernard A., 533

Hosten, Adrian O., 597

Jaffurs, William J., 497, 499

Janicki, Bernard W., 115

Jannotta, Frank S., 389

Kanda, Louis T., 543

Keshishian, John M., 257

Klingenmaier, C. Herman, 107

Koulouris, Spiros, 193

Kushner, David H., 491

Lawrence, William H., 409

Lederman, Martin E., 359

Levin, Richard L., 124

Lewis, Jonathan A., 15

Lilly, John R., 341

Lindsay, Joseph Jr., 395

Luke, James L., 175

MacMillan, Robert M., 9

Marlow, John L., 503

Marsh, H. Brandis, 245

Martz, Douglas G., 497, 499

Micheli, Lyle J., 21

Middleton, Philip, 451

Mispireta, Luis A., 233, 241, 245, 251, 285, 543

Mock, Joseph, 543

Mroczek, William J., 437

Muniagurria, Alberto J., 295

Newball, Harold H., 111

Oberman, J. Wm., 353

Obma, Robert, 413

Oldt, Nevin, 359

Parks, Marshall M., 359

Patterson, Robert H., 389

Perry, Lowell W., 413

Pierce, Lawrence E., 124

Qazi, Anjum G., 251

Randolph, Judson G., 341

Rockoff, S. David, 129

Russo, John V., 251

Salazar, Fernando A., 533

Schillaci, R. F., 457

Scott, Lewis P., 413

Sherer, Peter B., 66

Silver, Harold M., 120

Simon, David, 197

Sloan, Alexander M., 1

Smyth, Nicholas P. D., 257

Spero, Charles, 553

Steinglass, Peter, 183

Stevens, Harold, 593

Stewart, Steele, 497

Stueber, Kristin, 237

Sybert, Allender, 295

Tarjan, Peter, 257

Thong, Y. H., 63

Trujillo, Nelson P., 553

Tunell, William P., 341

Vieweg, W. V. R., 457

Wherry, David C., 189

Wilson, Margene, 437

Witorsch, Philip, 124

Wolin, Steven J., 183

Zehner, Harry Jr., 189

Zimmerman, Jack E., 107

Scientific Articles

- Actinomycosis Arthritis: A Case Report (Sherer, Dobbins), 66
- Asymptomatic Mullerian Anomalies (Currie), 18
- Benign Recurrent Cholestasis: A Manifestation of Pancreatitis (Salazar, Heckman, Dobbins, Danovitch), 533
- Bilateral Successive Adrenal Pheochromocytoma With Complicating Essential Hypertension (Doromal Middleton), 451
- Busulfan Lung Complicated by Pneumocystis carinii and Cytomegalovirus Infection (Green, Levin, Pierce, Witorsch), 124
- Carotid Artery Replacement with a Saphenous Vein Graft for Other Than Arteriosclerotic Obstructive Disease (Stueber, Garro, Absolon), 237
- A Case Report of Serratia Endocarditis with Review of the Literature (Farhoudi, Banks, Ali), 401
- Colonoscopy-Fiberoptic Endoscopic Approach to the Colon and Polypectomy (Wherry, Zehner), 189
- Colposcopic Evaluation of Stilvestrol Exposed Young Women (Marlow), 503
- Complications of External Cardiac Resuscitation: A retrospective review and survey of the literature (Patterson, Burns, Jannotta), 389
- Continuous Infusion of Diazepam in Infants with Severe Recurrent Convulsions (Thong, Abramson), 63
- The Definitive Diagnosis and Treatment of Pulmonary Disease by Selective Bronchial Catheterization (Rockoff), 129
- Diagnosis and Treatment of Hemodynamic Abnormalities after Acute Myocardial Infarction (Gorfinkel, Haider, Lindsay), 395
- Experiences with Transportation of the High-Risk Newborn (Blackburn, Edwards, Fletcher, Avery), 349
- Five Year Followup of Colonic Transplants in Patients with Epidermolysis Bullosa Producing Esophageal Obstruction (DeLeon, Mispireta, Absolon), 241
- The Frequency and Fate of Pregnancy After Age 45 (Kushner), 491
- Hepatic Artery-Portal Vein Fistula with Hepatic Cirrhosis, Hepatoma and Bleeding Esophageal Varices (Kanda, Mispireta, Mock, Absolon), 543
- Hypertension Detection in Existing Outpatient Clinics of Metropolitan Washington, D.C. (Mroczek, Wilson, Finerty), 437
- Hypertensive Cerebellar Hemorrhage (Lawrence), 409
- Immunologic Studies in Nitrofurantoin Induced Pulmonary Disease (Goldstein, Janicki), 115
- Interactional Behavior in An Alcoholic Community (Wolin, Steinglass), 183
- Intraventricular Hematoma Successfully Treated by Surgery (Koulouris, Fatehi, Cooney), 193
- Isolated Agenesis of the Right Pulmonary Artery Terminating in Pneumonia in a Young Adult (Vieweg, Conte, Schillaci), 457
- Leiomyomata with Aplasia of the Uterus and Fallopian Tubes: A Case Report (Cromer, Jaffurs, Martz), 499
- Loose vs Tight Fitting of Silastic Prosthesis of the MP Joint of the Hand (Lewis), 15
- The Management of Spine Deformities in the Myelomeningocele Patient (Michell, Hall), 21
- Lesenteric Vascular Disease: Clinical Features and Review of the Literature (Muniagurria, Sybert), 295
- Mixed Mesodermal Tumors of the Corpus Uteri (Jaffurs, Martz, Stewart, Cromer), 497
- The Morphology, Physiology and Therapy of Mitral Valve Disease with Giant Left Atria (Qazi, Mispireta, Russo, Bacos, Absolon), 251
- Multiple Excavating Pulmonary Metastases (Simon), 197
- Opiate "Overdose" Deaths in the District of Columbia 1. Heroin-Related Fatalities (Greene, Luke, DuPont), 175
- Peripheral Coronary Artery Perfusion for Direct Coronary Artery Reconstruction (Freant, Mispireta, Absolon), 233
- Physiological Rationale for the Clinical Use of Low Output Pacemakers (Smyth, Keshishian, Baker, Tarjan), 257
- Pneumothorax During Respirator Therapy (Zimmerman, Dunbar, Klingenmaier), 107
- Possible Coagulation Defects Seen in Rocky Mountain Spotted Fever (Driggers), 25
- Premature Menopause: A Report of Two Cases (Falk), 493
- Primary Hyperparathyroidism (Mispireta, Doromal, Diaz), 285
- Primary Linitis Plastica Carcinoma of the Colon (Bashour, Goldman, Gerber, Danovitch), 549
- Psychological Aspects of Intensive Care Units (Abram), 59
- Response of Asthmatic Airways to Intravenous Bradykinin and Histamine (Newball), 111
- Selective Hypoadosteronism: A Case Report and Review of Literature (Cruz, Dillard, Hosten), 597
- Subjective Response to Therapy in Chronic Obstructive Lung Disease (Silver, Eaton), 120
- Surgical (and Medical) Sequelae of Drug Addiction (Geelhoed), 307
- A Survey of Immunization Status of Children Enrolled in a Comprehensive Health Clinic (Oberman), 353
- Sympathetic Beta Adrenergic Blockade in the Preoperative Treatment of Hyperthyroidism (Brody, Dibble), 72
- Syncope Associated with Esophageal Stricture (Trujillo, Spero), 553
- Thermal Burns in Children (Randolph, Tunell, Lilly), 341
- Torsion of the Testis and Its Appendages (Geelhoed), 441
- Transient Global Amnesia (Stevens, Ammerman), 593
- Treatment of Parkinson's Disease with Carbidopa, A Peripheral Decarboxylase Inhibitor, and Levodopa (Fermaglich), 587
- Tumors of the Heart (Mispireta, Marsh, Bacos, Diaz, Absolon), 245
- Uhl's Anomaly of the Heart with Atrial Septal Defect and Valvular Pulmonary Stenosis (Obma, Perry, Scott), 413
- Unusual Abnormalities Associated with the Floppy Mitral

1974 INDEX

- Valve Syndrome (Daniels, D'Ambrosio, Bedynek), 4
 Uremic Constrictive Pericarditis (Sloan), 1
 Use of the High Plus Bausch and Lomb Soflens_® in the
 Management of Aphakia in Infants and Children (Friendly,
 Bruner, Frey, Lederman, Parks, Oldt), 359
 The Use of Immunosuppressive Agents in Takayasu's
 Arteritis (Alpert), 69
 Variant Angina Pectoris (MacMillan, Frankl), 9

Book Reviews—Authors

- | | | |
|---------------------------|-----------------------------|--------------------------------|
| Bala, Louis B., 51 | Moss, James M., 223 | Silby, Howard M., 51 |
| Berler, David K., 224 | Moxness, Bennie A., 279 | Snyder, James R., 51 |
| Bernstein, Howard N., 280 | Periman, Phillip, 169 | Stubenbord, John, 99, 279, 485 |
| Danovitch, Stuart H., 99 | Phelps, Elbert T., 52 | Tievsky, George, 382 |
| DuPont, Robert Jr., 52 | Rios-Pradier, Jorge C., 381 | Weintraub, William H., 578 |
| Gillis, Richard, 223 | Ruskin, Arthur, 169 | Weiss, Edward H., 525 |
| Herrera, Hector H., 525 | Sappington, Thomas S., 381 | Weiszer, Isaac, 577 |
| Hirsh, Harold L., 100 | Shnider, Bruce I., 101 | Zehner, Harry Jr., 224 |
| Lemp, Michael A., 485 | | |

Book Reviews

- | | |
|--|---|
| Aging and Mental Health. Robert N. Butler, M.D. and Myrna I. Lewis. (Stubenbord), 99 | P. Ellis, M.D. and Donald Smith, M.D., Ph.D. (Bernstein), 280 |
| Allergy Management in Clinical Practice. Louis Tuft, M.D. (Weiszer), 577 | Labor-Management Relations in the Health Services Industry. Norman Metzger and Dennis D. Pointer. (Hirsh), 100 |
| The American Heroin Empire, Power, Profits and Politics. Richard Kunnes, M.D. (DuPont), 52 | Major Modalities in the Treatment of Drug Abuse. Leon Brill and Louis Lieberman, Editors. (DuPont), 52 |
| The American Medical Machine. Senator Abraham Ribicoff with Paul Danaceau. (Phelps), 52 | Malnutrition—Its Causation and Control. Volumes I and II. John K. Robson. (Moss), 223 |
| Before Addiction: How to Help Youth. Florence Lieberman, Phyllis Caroff and Mary Gottesfeld. (Stubenbord), 485 | Manual of Cardiac Arrhythmias. Michael Bilitch, M.D. (Rios-Pradier), 381 |
| Clinical Aspects of Thromboembolism. W.R. Pitney, M.D. (Moxness), 279 | Medical Education in the United States Before the Civil War. William Frederick Norwood. (Shnider), 101 |
| Clinical Electroneurography. Mario P. Smorto and John V. Basmajian. (Silby), 51 | Neuro-Ophthalmology, Volume VII. J. Lawton Smith and Joel S. Glaser. (Berler), 224 |
| Corneal Graft Failure. Edited by B.R. Jones. (Lemp), 485 | The Newborn Chest. L. Wesenberg, M.D. (Weintraub), 578 |
| The Drug Abuse Controversy. Clinton C. Brown, Ph.D. and Charles Savage, M.D., Editors. (Ruskin), 169 | Patterns in Forcible Rape. Menachem Amir. (Weiss), 525 |
| Gastroesophageal Reflux in Hiatal Hernia. David B. Skinner, M.D., Ronald H. R. Belsey, Thomas R. Hendrix, M.D. and George D. Zuidema, M.D. (Danovitch), 99 | Pediatric Otolaryngology. Charles F. Ferguson, M.D. and Edwin L. Kendig, Jr., M.D., Editors. (Balla), 51 |
| Gastrointestinal Pathology. Basil C. Morson and I.M.P. Dawson. (Sappington), 381 | Pharmacology-Drug Actions and Reactions. Ruth R. Levin, Ph.D. (Gillis), 223 |
| Genetic Control of Immune Responsiveness. Hugo O. McDavitt and Maurice Landy, Editors. (Periman), 169 | Rise Up to Life. Leonard Bickel. (Stubenbord), 279 |
| Hamilton Bailey's Demonstrations of Physical Signs in Clinical Surgery. Allen Crain, Editor. (Zehner), 224 | Statistics in Small Doses. Winifred M. Castel. (Snyder), 51 |
| Handbook of Ocular Therapeutics and Pharmacology. Philip | Ureteral Dynamics, Pathophysiology, Drugs and Surgical Implications. Saul Boyarsky, M.D. and Peregrina Labay, M.D. (Herrera), 525 |
| | The Use of X-ray Techniques in Forensic Investigations. Daniel Graham. (Tievsky), 382 |

Special Articles—Authors

- | | | |
|-----------------------------|--------------------------|---------------------------|
| Bernton, Horace W., 445 | Moyer, Paul R., 317 | Walker, Bailus, 603 |
| Fairbanks, David, 367 | Price, Melba, 603 | Wallenberg, Ellis A., 367 |
| Funderburk, William W., 407 | Squires, Russell D., 317 | Webb, Blair M., 367 |
| Karpick, Ronald J., 137 | | |

Special Articles

Acupuncture for Deafness: A Study of Patients Treated in Washington, D.C. (Fairbanks, Wallenberg, Webb), 367
 Causes of Death Soon After Injury (Funderburk), 407
 HMO—Friend or Foe? (Bernton), 445
 PSRO, SSA and Private Practice of Medicine (Squires,

Moyer), 317

Public Behavior During an Air Pollution Episode: Implications for Health Planning (Price, Walker), 603

Recent Advances in Respiratory Therapy (Karpick), 137

General

ECG Problems (Montgomery), 8, 150, 188, 250, 306, 352, 412, 502, 575, 592

Gruver, Clifton R., President of the Medical Society of D.C., biography, 41

Medical Society Officers and Committees for 1974, 159
 Post Graduate Education

The Use of Liver Function Tests (Danovitch), 45

Adult Respiratory Distress Syndrome (Canter), 93

Prudent Nutrition and the Pill (Giere), 147

Medical Management of Rheumatoid Arthritis (Sliwinski), 217

When to Consider Coronary Artery Bypass Surgery (Shugoll), 429

Treatment of Malabsorption Syndromes (Horrigan), December, 5.

The Systolic Click—Late Systolic Murmur Syndrome (Ronan), December, 13.

Smith, Robert B. W., Editor, *Medical Annals of the District of Columbia*, biography, 41

The View Box (Augustin), 14, 110, 182, 236, 294, 348, 411, 444, 496, 542

INDEX TO ADVERTISERS

Insurance

Corroon & Black, Russell, Inc. 17
 Ralph W. Lee & Company 4
 Mutual of Omaha 11

Nurse Registries

District of Columbia Manpower
 Administration T-622
 Visiting Nurses Association 12

Nutrition Education

Dairy Council of Greater Metropolitan
 Washington, D.C. 2

Pharmaceuticals

Burroughs Wellcome & Company T-609

Dorsey Laboratories 7, T-613
 Eli Lilly & Company 18
 Pharmaceutical Manufacturers
 Association T-610-T-611
 William P. Poythress & Company 8
 Roche Laboratories C2, 1, C3, C4

Pharmacy

Peoples Drug Stores T-612

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Suter Associates Retirement Planning Company 17

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